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MEDICAL MANAGEMENT OF THROMBOPHLEBITIS AND POSTPHLEBITIC SYNDROME

SURVEY OF FOUR HUNDRED TREATED CASES FROM A SERIES OF SEVEN HUNDRED SEVENTY-NINE CONSECUTIVE CASES OF PHLEBITIS

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The outcome in any case of thrombophlebitis is unpredictable, but fortunately a vast majority of the cases can be controlled with proper management. Even if the phlebitis is localized in a small area, that patient should have maximum therapy because the tendency to develop complications and sequelae exists and further developments of the pathological process are unpredictable. Prompt and thorough treatment in these cases may bring about a more rapid favorable control and lessen the tendency for the condition to spread and recur, and has a definite influence on curtailing the incidence of the postphlebitic syndrome. Hospitalization is recommended for all patients with thrombophlebitis, those with the mild as well as the more severe forms. Subsequent care of phlebitis is an important aspect of the general management in order to avoid recurrences as well as to prevent the postphlebitic syndrome.

THE subject of thrombophlebitis, because of the increasing incidence of this disease, demands consideration from various angles. A recent survey of 2,300 consecutive case records [1] showed 779 cases of phlebitis; in 631 cases, patients had evidence of thrombophlebitis and, in 148, patients were listed as having the postphlebitic syndrome. A further examination of these records indicated that, of the 631 cases of thrombophlebitis, 300 patients had been treated and observed for some time and 100 of the postphlebitic group had likewise received intensive therapy.

An analysis of the effect of the treatment in the 400 cases revealed some interesting and striking data, which indicated that thorough and complete treatment not only produced good results in a high percentage of the cases but also was instrumental in containing the condition and preventing complications and sequelae which may occur in patients with this disease.

Methods of Grading Results

Any method of evaluating the results of therapy must be arbitrary and probably will not be acceptable to everyone. Many tangibles enter into the

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problem and cannot be brushed aside without some consideration. Review of the records revealed patients in whom the thrombophlebitis was completely controlled, but in whom, six months or a year later, an episode of thrombophlebitis occurred in another extremity, or occasionally in the same area as a result of an injury or a systemic infection. This certainly could not be listed as a failure.

However, some method of grading the results must be formulated, even if it is not completely satisfactory, in order to obtain a comprehensive idea whether therapy is beneficial and to what extent it has helped the patient. The following method of scoring was adopted. In the thrombophlebitis group, a good result was recorded if the active thrombophlebitis was controlled, evidenced by the relief of pain and the disappearance of swelling and all signs of inflammation, both local and systemic. An improved grade was recorded if there were evidences of improvement, both subjectively and objectively, but the phlebitis was not completely and satisfactorily controlled. If the phlebitis persisted or extended and involved other areas despite a reasonable course of treatment, the result was listed as a failure.

TABLE 1.—*Etiological Factors, Sex, and Site in Thrombophlebitis and Postphlebitic Syndrome Groups*

	Thrombophlebitis (300 Cases)	Postphlebitic Syndrome (100 Cases)	Total
Etiology			
Trauma	80	29	109
Infection	104	35	139
Postoperative state	16	11	27
Pregnancy	23	12	35
Blood dyscrasia	5	...	5
Malignancy	2	1	3
Indefinite	85	15	100
Site			
Right	115	25	140
Left	132	48	180
Bilateral	53	27	80
Sex			
Male	133	45	178
Female	167	55	222

The postphlebitic syndrome group presented some difficulties in scoring the results of therapy because of the extensiveness of the condition and the vulnerability of the tissues. A good result was recorded if the inflammatory process was contained, with the swelling considerably reduced to a minimal degree, complete subsidence of the dermatitis, relief of pain, and healing of the ulcer (if one was present). If the above qualifications were not complete but therapy indicated that the patient was benefited in many respects, such as healing of an ulcer or other evidences of controlling the underlying pathological changes in the extremity, such cases were listed as improved. Where there was little or no improvement, such cases were reported as failures. The results of therapy in our series will be discussed subsequently.

Etiology

Before taking up the subject of treatment, it may be pertinent to briefly comment upon the various factors which cause thrombophlebitis and enumerate the various sequelae and complications which may develop in an episode of recurring attacks of thrombophlebitis.

It is not necessary to go into details of the etiology of thrombophlebitis.[2] However, the following influences may be mentioned, such as trauma of the intima from various causes; infection, local or systemic; slowing down of the blood flow; and changes in the blood cellular elements, such as the red blood cells (polycythemia) and the platelets increasing in number and adhesiveness. Contributory factors are the postoperative state, pregnancy, puerperium, systemic infections, fractures of long bones (particularly in the aged), blood dyscrasia, malignancy, constitutional liability, and possibly some metabolic factors. The data in table 1 were obtained from an analysis of the 400 treated cases from both groups.

Complications and Sequelae of Thrombophlebitis

The outcome in any case of thrombophlebitis is unpredictable. Fortunately a vast majority of the cases can be controlled with proper management.[3] However, a variety of developments may occur, such as extension of the thrombosis by continuity; involvement of other veins, either in the same extremity or in other extremities, due to some unexplainable factor; extension of the inflammatory process upward and involvement of the valves; pulmonary infarction; fatal pulmonary embolism; in rare instances, suppuration of the involved vein; perivenous inflammation; involvement of the lymphatics with possible permanent damage to the channels; occasionally, thrombosis of the adjoining artery; and, in exceptional cases, gangrene resulting from involvement of the large venous trunks.

If these episodes occur frequently enough or if the primary episode is a severe one, resulting in damage to the valves and marked perivenous inflammatory reaction, the postphlebitic syndrome may develop. In such cases, the basic clinical picture is one of chronic venous insufficiency with the hazards of recurring episodes of thrombophlebitis, cellulitis and lymphangitis, persistent edema, stasis dermatitis, and ulcers. Needless to say, all of the above-mentioned manifestations need not be present. However, in severe cases, where there have been recurring episodes of thrombophlebitis and perivenous inflammation, the entire clinical picture may ultimately present itself.

Treatment

Therapy should be instituted promptly, and it should be as thorough and complete as possible.[4] This rule should be carried out regardless of the site and extent of the involvement. Even if the

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phlebitis is localized in a small area, that patient should have maximum therapy because the tendency to develop complications and sequelae exists and further developments of the pathological process are unpredictable. Prompt and thorough treatment in these cases may bring about a more rapid favorable control and lessen the tendency for the condition to spread and recur, and, in our experience, has had a definite influence upon curtailing the incidence of the postphlebitic syndrome. The subject of treatment will be divided into (1) management of thrombophlebitis and subsequent care and (2) treatment of the postphlebitic syndrome with its subsequent care.

Treatment of Thrombophlebitis.—Hospitalization is recommended for all patients with thrombophlebitis, those with the mild as well as the more severe forms. The following regimen is instituted:

1. The patient must rest in bed.

2. Elevation of the injured limb may be accomplished with pillows or, preferably, by raising the foot of the bed 6 to 8 in. with blocks.

3. Paravertebral block with 1% solution of procaine hydrochloride is particularly helpful in cases where there is considerable edema and pain. By this procedure, the pain is relieved and there is a striking subsidence of the edema within 24 to 36 hours. However, a paravertebral block, if it can be arranged, should be done before anticoagulant therapy is instituted. If anticoagulants have already been administered, paravertebral block is inadvisable, because it may result in hemorrhagic extravasation and exacerbation of the thrombophlebitis.

4. Continuous warm wet compresses over the entire extremity have a favorable effect upon the vasospasm, and the patients usually feel more comfortable with them. When possible, a large electric cradle may be helpful in maintaining the continued warmth which is desirable.

5. Anticoagulant therapy has been universally adopted and needs no further elaboration in this presentation. At the onset of the treatment and particularly in severe cases, heparin is recommended. This may be given either in the aqueous solution of 100 mg. twice daily for the first 24 hours or as a repository dose of 300 mg. intramuscularly. At the same time, bishydroxycoumarin (Dicumarol) therapy may be started by giving 300 mg. orally; the daily dosage thereafter is gauged by estimations of prothrombin time. A chart indicating the prothrombin time and the dose of bishydroxycoumarin is kept daily. We have found it useful to employ the following dosage guide, so that the bishydroxycoumarin may be given without requiring the presence of the attending physician: The dose of bishydroxycoumarin is 200 mg. if prothrombin time is 90 to 100 %; 100 mg. if 70 to 89%; 75 mg. if 50 to 69%; 50 mg. if 30 to 49%; and 25 mg. if 20 to 29%. No bishydroxycoumarin is given if prothrombin time is below 20%.

6. Depropanex, an insulin-free extract of the pancreas, is given intramuscularly for vasodilation in doses of 1 to 2 cc. daily. Nylidrin (Arlidin), 6 mg., or tolazoline (Priscoline), 25 to 50 mg., given orally three times a day before meals, is prescribed, and papaverine hydrochloride, 1 grain, (60 mg.), four times a day after meals and at bedtime. Papaverine may be given orally, but, in acute cases, the subcutaneous route is recommended.

7. Salicylates with codeine, ¼ to ½ grain (15 to 30 mg.) every four hours, may be given as an analgesic. If pain is severe, meperidine (Demerol), 25 to 50 mg., is recommended for the patient's comfort.

8. Secobarbital (Seconal) or pentobarbital (Nembutal), 1½ grain (0.1 Gm.), or any of the barbiturates may be prescribed if sedation is necessary.

9. In the presence of fever and evidence of an acute inflammatory condition, antibiotics may be helpful. Although this has been a routine procedure, the results of antibiotic therapy have not been too encouraging.

10. Physical medicine procedures are instituted after the edema has subsided. Methacholine (Mecholyl) chloride, administered by iontophoresis,[5] the immersion or spiral electrode method, is given every other day for a series of 10 treatments. This procedure has been very helpful in overcoming the arteriolar spasm and venous spasm, as well. The oscillating (Sanders) bed is prescribed routinely in these cases for one hour or more daily during the patient's stay in the hospital. The pavex or glass boot is definitely contraindicated in these cases because of the liability of producing an exacerbation of the thrombophlebitis and because it may have a deleterious effect upon the weakened veins. Intermittent venous compression may be used. However, it is not as satisfactory as the oscillating bed. It is contraindicated in the presence of edema.

11. If epidermophytosis is present, the usual measures directed to control this condition are prescribed, i.e., foot soaks with potassium permanganate solution (1:5,000) or application of compound undecylenic acid ointment (Desenex)[6] or carbolfuchsin solution (Castellani's paint).

Subsequent Care: Subsequent care in these cases is very important and too often neglected. After the edema has subsided and the patient is ready for ambulation, elastic support is ordered while he is out of bed. Preferably, an elastic bandage should be employed and should extend from the toes up to midthigh or higher. Later, when all evidence of edema has been controlled, an elastic stocking may be substituted. The elastic support should be continued for at least three to six months or longer, if indicated. The patient is instructed to sleep with the feet elevated.

Anticoagulant therapy should be continued for at least three months, and longer if necessary. Bishydroxycoumarin therapy will be guided by the estimations of prothrombin time. During the patient's

stay in the hospital, one can readily ascertain the daily dosage of bishydroxycoumarin necessary to maintain satisfactory prothrombin levels. In ambulatory cases, however, frequent or daily estimations of prothrombin time may not be feasible, and the physician in charge must learn to regulate the dose reasonably well with weekly blood studies. Although prothrombin time levels of 20 to 30% are preferable for optimal therapeutic effect, this need not be insisted upon in ambulatory cases. Levels below 50% may be sufficient. Later, as some definite standard has been reached with the same dosage of bishydroxycoumarin, the estimations of prothrombin time may be done every two weeks. In these cases, as a rule, 50 mg. daily has been found to be a good average dose.

Obviously, the patient is instructed to report any sign of hemorrhagic extravasations in the subcutaneous tissues or hematuria; these are the usual manifestations seen when the prothrombin time drops to extremely low levels. Fortunately, it is not a frequent occurrence and may readily be controlled by discontinuing the bishydroxycoumarin and giving vitamin K therapy, by intramuscular injection, orally, or, in acute cases, intravenously. If the patient has had a profuse hemorrhage, it may be necessary to give transfusions, preferably with fresh blood.

Vasodilators are continued, nylidrin, tolazoline, or nicotinic acid and papaverine, in the usually accepted doses. Periodic treatments with methacholine administered by iontophoresis and with the oscillating bed are continued for a series of 10 treatments once weekly and, later, once every two weeks. Patients are instructed to avoid trauma or too great a demand upon the legs until they have fully recuperated and are able to carry on their regular duties. They are also instructed to give immediate attention to any trivial injuries or colds.

Some patients, who have a tendency for upper respiratory infections which preceded the episodes of phlebitis, are placed on prolonged antibiotic therapy, penicillin, 100,000 to 200,000 units, or sulfonamide compounds, 0.5 mg. daily, as preventive measures. This may not be necessary for the average patient but, when indicated, may be very helpful in preventing recurrences.

Treatment of the Postphlebitic Syndrome.—The management of patients with postphlebitic syndrome is basically similar to the regimen outlined for acute thrombophlebitis, namely, rest in bed; elevation; therapy with anticoagulants, vasodilators, antibiotics, and analgesics; continuous warm wet compresses; and electric cradle. In addition, other measures are employed in an attempt to control the various complicating factors which may be present. There has been considerable interest in the employment of enzymes in inflammatory conditions. Trypsin has proved to be very helpful in such cases.[7] Originally, it was used by the intravenous route, where it could exert a more direct effect upon the involved areas. However, because of the possible toxic effects, this was discontinued. It is generally used intramuscularly. Preparations of trypsin, such as Parenzyme and Chymar, are given in doses of 5 mg. once daily or 2.5 mg. twice daily. Investigations have shown that trypsin has a favorable effect by reversing the inflammatory reactions of tissues. Numerous contributions have proved its value in edema, cellulitis, and particularly in hemorrhagic extravasations in the tissues.

Another preparation, which has been very helpful in our experience, is tetraethylammonium (Etamon) chloride, which is an autonomic blocker.[8] It has been used in patients who have persistent pain and who have ulcers that have not responded to therapy. It may be given intravenously in doses of from 300 to 400 mg. daily. However, the intramuscular route is less apt to cause side-effects. When given in this manner, larger doses may be used, from 500 to 600 mg. daily, divided in two doses, injected in the gluteal region on each side. A series of 5 to 10 injections should be sufficient. It is not advisable to give it indefinitely.

In the presence of cellulitis and lymphangitis, antibiotics of the various spectrums are given by intramuscular injection at the onset of the treatment and, if necessary, may be continued orally, as indicated. If there is a marked dermatitis or cellulitis, nonirritating solutions may be recommended in the form of compresses, with use of a weak boric acid solution or isotonic sodium chloride solution.

If, despite all measures, there is evidence of spreading of the thrombophlebitis or recurrence in other areas and evidence of marked perivenous inflammatory reaction, it may be necessary to resort to foreign protein therapy.[9] Typhoid vaccine is employed. A series of five injections is given, in doses starting with 25 million organisms and gradually increasing to 50, 75, 100, and then 150 million organisms. The sequence of the injections may be given after 24-hour intervals of normal temperature. The details of this procedure can be obtained in textbooks. Foreign protein injections are helpful in patients with recurring infectious thrombophlebitis, and particularly in cases associated with thromboangiitis obliterans or where there is an extension of the pathological process.

For the dermatitis and eczematous dermatitis, soothing lotions are usually prescribed, containing calamine (zinc oxide in an oil base). Strong, irritating solutions should be avoided.

Ulcers are treated routinely in the manner described above with the addition of some local therapy, such as dilute solutions of antibiotics (tyrothricin [Soluthricin], 0.5%, or bacitracin) applied topically. Continuous wet dressings are not encouraged and ointments may only be used as a temporary measure. The electric cradle with a 25-watt

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bulb may be helpful. Frequent cleansing and removal of dried secretions is beneficial. In persistent chronic ulcers with sloughing, particularly with scab formation, streptokinase-streptodornase (Varidase) may be helpful. This should be employed with an applicator and limited to the involved area only. It is used daily for a limited time, three to five days.

The various physical medicine procedures are very helpful in these cases. When the acute inflammatory condition is under control and the fever has subsided, physical medicine procedures are instituted, such as administration of methacholine by iontophoresis every other day and use of the oscillating bed daily for a series of 10 treatments.

Subsequent Care: A patient with postphlebitic syndrome will usually improve sufficiently to be permitted to ambulate after a period of three to four weeks of therapy. After his discharge from the hospital, he is instructed to wear an elastic support for three to six months while he is up and about. He should be advised to gradually resume his activities and avoid excessive demands upon his venous circulation. He should avoid unnecessary exposure to infection and should give immediate attention to trivial injuries. He is advised to sleep with his limb elevated, either on pillows or by raising the foot of the bed with wood blocks. If there is a history of an upper respiratory infection preceding episodes of recurring thrombophlebitis, the patient is advised to take daily doses of penicillin, with or without sulfonamides, for an indefinite period. He is requested to report to the office for subsequent care, where he is given a series of 10 treatments, once weekly or every two weeks, consisting of administration of methacholine by iontophoresis, use of the oscillating bed, and intramuscular injections of Depropanex. Therapy with vasodilators is continued indefinitely, with either mylidrin or tolazoline and papaverine. Anticoagulants are continued for at least three to six months and, in some cases, patients have been carried along for years, if necessary, on small doses (25 to 50 mg. of bishydroxycoumarin).

The possible role of diet in the management of arterial disorders, particularly atheromatosis, has been conceded. The high incidence of vascular complications occurring in diabetics has been recognized factually. In such cases, carbohydrate and cholesterol metabolism is entailed. However, upon observing the blood uric acid determinations in a number of the phlebitis cases, it was noted that many had what may be termed high normal levels and it was not uncommon to find levels above normal. These findings are being reviewed and will be published subsequently.

Obviously, the condition of patients with phlebitis with a diabetic background must be rigidly controlled with diet and insulin, if necessary. If there is evidence of hypercholesteremia, a low-fat and low-cholesterol diet is recommended. Patients who have high uric acid determinations are placed on a low-purine diet, and colchicine in small doses is prescribed for prolonged periods, if indicated. Low-calorie diets are prescribed routinely in the overweight individuals. Weight reduction in the obese patients is advisable for obvious reasons.

The significance of the above suggestions for diet is further enhanced when we consider that in a number of cases where there is evidence of atheromatous changes in the arteries this may bring about some favorable influence upon the vessel walls. Low-calorie diet with weight reduction helps lessen the demands placed upon the lower extremities, and the low-purine diet may have some beneficial effect in preventing further pathological changes in the vessels. This is speculative, however, because the role of purine metabolism and uric acid metabolism upon the arteries is an entirely new concept which is now being considered in circulatory disturbances.

TABLE 2.—*Results of Therapy in Thrombophlebitis and Postphlebitic Syndrome Groups and Periods of Observation*

	Thrombophlebitis (300 Cases)		Postphlebitic Syndrome (100 Cases)		Total	
	No.	%	No.	%	No.	%
Results of treatment						
Good	209	69.6	53	53	262	65.5
Improved	82	27.4	35	35	117	28.3
Failures	9	3.0	12	12	21	6.2
Observation period (yr.)						
Less than 1	149		55		204	
1 to 3	84		21		105	
4 to 5	31		18		49	
6 to 10	19		4		23	
More than 10	17		2		19	

Comment

The treatment which has been described in detail is directed to contain the inflammatory process, overcome spasm of the veins as well as the arteries, and improve the circulation, whereby the increased blood flow acts as a deterrent to thrombosis. The subsequent follow-up therapy is aimed at maintaining this improvement for a prolonged time and very likely will keep the incidence of postphlebitic syndrome to a minimum.

The effects of treatment upon these cases were checked (table 2); results were arranged in three grades: good, improved, and failures. The first group included patients who appeared with their first attack of thrombophlebitis or who may have had previous episodes, but in whom the disease did not develop into the permanent clinical picture of the postphlebitic syndrome. Of the 300 cases of thrombophlebitis, results were good in 209 cases (69.6%); improved in 82 (27.4%); and failures in 9 (3%). A total of 291 patients (97%) were benefited in various degrees.

Naturally, the question may be posed as to how long a period the beneficial effects of therapy were maintained. Most of these cases were followed up

for various lengths of time. The majority of them were observed for periods up to one year, many up to 5 years, and some up to 10 years or even longer.

The postphlebitic syndrome group showed a smaller percentage of good results, which is to be expected since we are dealing with a chronic type of vein disorder and practically all of these patients had developed the condition before they reported for therapy. However, results were good in 53% of these cases, benefit in various degrees was achieved in 35%, and there were 12% failures.

The combined groups of both thrombophlebitis and postphlebitic syndrome showed good results in 262 cases (65.5%), an improvement in 117 cases (28.3%), and failures in 21 cases (6.2%).

The high percentage of satisfactory results, both the good and the improved cases, may be attributed to various factors. Hospitalization is recommended in all cases whether they are mild or severe, which permits complete and intensive therapy in order to obtain all the objectives, namely, (1) control of the inflammatory process, (2) overcoming the vasospasm, (3) instituting anticoagulant therapy, and (4) carrying out of the various physical measures, particularly administration of methacholine by iontophoresis and use of the oscillating bed.

Subsequent care is a very important aspect of the management if we are to avoid recurrences and if we are to eventually control or prevent the postphlebitic syndrome. Only in exceptional cases has the postphlebitic syndrome developed in those patients who received complete therapy and subsequent care.

Another factor is that, in carrying out the intense and complete therapy, measures are directed to remove any possible etiological factor which may be detected. In the presence of an infection, antibiotics or sulfonamides are prescribed. If there is a metabolic disturbance in the background, this is also corrected; if there is an existing occlusive arterial disorder, this condition is likewise controlled or corrected, if possible, by the above therapy.

Since this presentation is of the medical conservative care of venous inflammatory conditions, we have purposely avoided alluding to the various surgical procedures which have been offered in these cases.[10] Ligation of the large saphenous or femoral veins and stripping have been recommended in many articles. It certainly does not apply to the first episode of an acute thrombophlebitis and it is questionable in our opinion whether it should be the treatment of choice in the postphlebitic syndrome unless definitely indicated. It may be considered in some cases, where varicose veins of long duration are the primary source for the development of the inflammatory episodes, but this is not the usual story in our experience. Various surgical techniques have been offered to correct the postphlebitic syndrome. Bauer [10a] has pointed out the particular value of ligating and resecting the popliteal vein. We have no information from personal experiences with this procedure. However, his reports are of interest and deserve consideration.

In some cases where there is repeated pulmonary infarction, despite therapy, and where there is evidence of involvement of the large deep veins, such as the iliofemorals, ligation of the postcava has been recommended. In selected cases, this procedure may be advisable.

Summary

The problems of controlling inflammatory conditions of the veins deserve serious consideration. The management of thrombophlebitis has developed sufficiently to produce gratifying results. Treatment should be intensive, complete, and followed up. Hospitalization is recommended for all cases, mild as well as the severe or chronic forms. The routine therapy has been outlined and the subsequent care has been emphasized.

Of the 400 treated cases, 300 were classified as primary thrombophlebitis (including some patients who had had previous recurring episodes), and 100 cases were of postphlebitic syndrome. Results of therapy indicated that good results were obtained in 262 cases, improvement in 117 cases, and failure in 21.

Explanations for the gratifying results were (1) intensive and complete treatment, which entailed therapy with anticoagulants and antibiotics and physical medicine, (2) measures to improve the arterial as well as the venous circulation, (3) an effort to remove the causative factor, if detected, (4) improvement of the general health, and (5) prolongation of therapy and sustaining of venous circulation until compensatory measures have been established.

Experience has demonstrated that complete, intensive, and over-all treatment not only contains the pathological disturbance of the veins but also, to a considerable degree, prevents recurrences and lessens the probability of developing postphlebitic syndrome.

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CHRONIC INTOLERABLE PAIN

DISCUSSION OF ITS MECHANISM AND REPORT OF EIGHT CASES TREATED WITH ELECTROSHOCK

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The effectiveness of electroshock therapy in relieving chronic, intractable pain is illustrated in the case histories of eight patients. In five of these, surgical measures for relief of the primary cause of pain were ineffective, and the suffering of the patients was so severe, that some neurosurgical procedure such as lobotomy seemed to be the only alternative to the continued use of narcotics. The use of electroshock is theoretically justified in cases where the pain is probably the accompaniment of activity in certain reverberating circuits in the nervous system. It was justified in the present series by the practical results, since these eight patients, with but one exception, were successfully rehabilitated. Many of the electroshock treatments were given on an outpatient basis. Criteria for the selection of suitable cases remain to be defined, but it is clear that some patients can be saved by this means from the necessity of choosing between neurosurgery and drug addiction.

Of the problems presented to the clinical neurologist, the evaluation and treatment of chronic pain syndromes is one of the most frequent and often the most difficult. This is in large part due to the variations in subjective response to pain and to the incomplete understanding there is regarding the underlying physiological and psychological mechanisms concerning pain.

While there has been a great deal published concerning pain and pain mechanisms, it is my experience that so far as treatment is concerned there is not much material available that will help the clinician in the management of a particular case unless it fits into the category of conditions in which neurosurgical intervention is beneficial, such as trigeminal neuralgia, causalgia, and intractable pain due to irreversible organic states, which may often be relieved by chordotomy or frontal lobotomy. Too often patients with intractable pain of indefinite cause are considered, sometimes in desperation, for lobotomy before other types of treatment have been adequately tried.

The neurophysiological work of Lorente de Nó [1] demonstrated that there was a neuronal pool interposed between the sensory and motor components of the spinal cord. This supplied a means by which temporal and spatial dispersion of input could take place, and the number of neurons making up the pool permits great variety in dispersion patterns from simple to complex. From his theory of a closed self-reexciting chain within this pool came the concept of self-sustaining pain patterns, or internuncial pool, as exemplified in causalgia. It has been further demonstrated that influences from other parts of the nervous system can alter the motor responses to a sensory stimulus, and studies of the reticular

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formation in the brain stem and spinal cord [2] demonstrate that it plays an important part in modifying activity within the internuncial pool.

It may, therefore, be postulated that in certain individuals recurring painful stimuli from the periphery set up reverberating circuits related to the central activating system which influence, and are in turn influenced by, the cerebral cortex so that there may develop a syndrome of chronic pain which is frequently incapacitating and often results in the excessive use of pain-relieving drugs. As in causalgia, the additional trauma of a surgical procedure upon the part affected only serves to increase the incoming stimuli and to reinforce the abnormal physiological process producing the sensation of pain. In line with this concept it seems likely and appears to have been demonstrated clinically that the various emotional reactions related to this state, namely, preoccupation with symptoms, introspection concerning among other things the memories of the pain and anticipation of the future, depression, and anxiety, as well as emotional stress brought on by other conflicts, also serve to reinforce the reverberating circuits and further perpetuate the disability.

Only a small percentage of individuals suffering from a painful disorder develop chronic intolerable pain. It is my conception that this is due largely to the emotional reaction of the individuals concerned. This is exemplified by the studies of Beecher [3] on the variable effects of placebos, which illustrate the strong influence of suggestion on the response of the individual to medication, and by studies on the group of individuals described as congenitally indifferent to pain.[4] In the latter group, pain is perceived normally but there is no apparent emotional reaction to it so that the painful stimuli are never unbearable. It seems likely that in these individuals, for some as yet unexplained reason, the cortical elements related to the reverberating circuits do not manifest any influence, so that chronic pain syndromes do not develop.

In view of this, one might postulate that chronic pain syndromes, i. e., sustained pain after the disappearance of the original impetus, cannot develop unless cortical components are involved. Thus I would add one more reciprocating factor to the three cited by Livingston,[5] who states, "If I were to translate this clinical interpretation into physiologic terms I would say that there were three reciprocating factors in the vicious cycle of the causalgic state: incoming impulses from the periphery; the internuncial pool activity; and the motor impulses from the lateral and anterior horn cells that are brought within the influence of the pool." It might be further postulated that the individual's response to treatment to the peripheral nerves, such as injections of procaine (Novocain) hydrochloride or sympathectomy, or to drug therapy or psychotherapy would depend in part on the nature and degree of cortical involvement in the reverberating circuits. The fact that in some instances it appears that the emotional disturbance preceded the development of the chronic pain syndrome and in others it seemed to stem from it is explained by this concept. It is, therefore, this uncertainty in evaluating the influence of pain on emotion or vice versa that makes these patients such difficult therapeutic problems.

A series of illustrative cases is presented. It should be emphasized that all these individuals were referred to me, usually after medical and surgical treatment had been ineffective over a prolonged period of time.

Report of Cases

Case 1.—A 47-year-old married woman had, seven years before hospital admission, suddenly developed epigastric pain with nausea and vomiting. This was relieved by a hypodermic injection of meperidine (Demerol) hydrochloride. Subsequently she had such attacks every three to six months until early in 1955, when they occurred every other night until she had a partial gastrectomy for duodenal ulcer on June 29, 1955. After surgery she was free of pain for five days; then she began to have pain daily. She described the pain as horrible. It was accompanied by marked hyperperistalsis and was relieved at first by one or two hypodermic injections of meperidine. Later the drug relieved the pain for a few hours only.

The case history revealed no evidence of any previous illness, and there was no evidence of emotional stress or instability. The patient had seen a number of physicians and had been thoroughly studied medically. When I first saw her, on Aug. 15, 1955, she was in a knee-chest position, crying with pain and pleading for meperidine. She was cooperative but agitated and depressed. No abnormal physical or neurological findings were noted. She had lost considerable weight.

Sanatorium care and electroshock therapy were recommended, but the husband was advised against this by medical friends. The patient was transferred to another hospital, where, after a medical checkup, she was referred to the psychiatric department. Psychotherapy was advised, but the patient was so ill she could not get to the doctor's office. She gradually became worse, and finally, on Sept. 22, 1955, she was admitted to a sanatorium for electroshock therapy. She improved rapidly and was discharged at her husband's insistence on Nov. 19, 1955, but was readmitted on Nov. 25 because of a recurrence of symptoms. She was subsequently discharged and readmitted twice. Her final discharge was July 28, 1956, since which time she has remained well. She had a total of 42 treatments.

This case illustrates development of chronic pain due to duodenal ulcer, increase of pain after gastric resection, and relief from pain with sanatorium care and electroshock therapy.

Case 2.—A 45-year-old woman was first seen on Jan. 8, 1954, because of abdominal pain, vomiting, malnutrition, and depression. She had been well until six years before when she had developed severe abdominal pain attributed to gallstones, which had been present for some time. Abdominal pain and vomiting persisted, and in December, 1951, she was given a diagnosis of inoperable carcinoma of the stomach. In January, 1953, gallbladder surgery was required, and exploration revealed an apparently normal stomach. However, she continued to have abdominal pain and vomiting and weighed only 84 lb. (38.1 kg.) when I first ex-

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amined her. At that time she complained of constant abdominal pain with spasms "just where the gallbladder was." She was unable to retain food, felt quite depressed, and was taking a considerable amount of meperidine for relief. The depression had apparently become evident when her youngest son had died two years before. The husband drank to excess and when intoxicated abused her. Examination revealed only evidence of marked loss of weight.

She was admitted to a sanatorium Jan. 16, 1954, where 12 electroshock treatments were administered. She improved and was discharged Feb. 18, at her insistence. She did not maintain her improvement at home. Abdominal pain and vomiting recurred. She was returned to a sanatorium on July 15, 1954, and given 17 more electroshock treatments. She improved markedly and was discharged on Sept. 16. She subsequently remained quite well and resumed many of her social activities and family responsibilities. She ate well and had no nausea, vomiting, or abdominal pain.

Late in 1955, after being under considerable emotional strain, she began to have abdominal distress similar to that she had had before. Sanatorium care was advised and refused. Subsequently outpatient electroshock therapy was given. She had 16 treatments, two to five days apart, with some improvement at first; then, however, her abdominal distress increased. She would not consider entering a hospital for study. Finally, on April 10, 1956, she became delirious, and she died shortly after entering the sanatorium. The autopsy showed acute bacterial nephritis with formation of multiple abscesses and a large chronic benign gastric ulcer.

This case illustrates the development of chronic abdominal pain as a result of the combination of intra-abdominal pathology and emotional stress. While the patient was quite depressed when first seen by me, it appeared that the abdominal distress had been present long before she had become depressed but had not been constant or incapacitating until she had become disturbed emotionally. There was marked improvement with sanatorium care and electroshock therapy.

Case 3.—A 55-year-old woman was examined on March 3, 1956, because of terrific thumping pain in the back of the neck and head, associated with vomiting which had been troubling her for three years. She had flashes of light before her eyes and loss of equilibrium, but no dizziness. She had lost consciousness with the first and several subsequent attacks. Her blood pressure had been markedly elevated each time she had had a headache, which usually lasted from a few days to several weeks. She was hospitalized "25" times in three years because of these complaints and had had "every kind" of medicament, even narcotics, without relief.

The case history revealed that the patient had been happily married for 36 years. She had had "migraine" for 10 years, but this had subsided 5 years before hospital admission. There had been eight major operations, none recently. When the patient had been 28 years of age she had had a hysterectomy, followed by nervousness and depression, which had been diagnosed as premature menopause.

No neurological abnormalities were noted. The patient was alert and cooperative and did not appear to be depressed even when she discussed her difficulties. It was at first felt that she might have migraine or a convulsive disorder with a psychoneurotic reaction. The electroencephalogram was negative. The patient did not improve, and, finally, after several conferences with her internist, electroshock therapy was instituted.

On admission to a sanatorium on March 12, 1956, she complained constantly of severe headache, until after the fourth electroshock treatment. She continued to improve and was discharged on April 13, 1956, having had 10 electroshock treatments. She got along well for about two months; then her headaches recurred, and she was readmitted June 5 and discharged, free of symptoms, July 21, having had 12 more electroshock treatments. Since then she has remained well.

This case illustrates the development without apparent cause of chronic head pain in a psychoneurotic individual. One might presume the patient's symptoms were the product of an emotional depression, though she did not appear to be particularly depressed. While the prognosis of the condition seemed unfavorable when the patient was first seen, she did very well with electroshock treatment and supportive psychotherapy.

Case 4.—A 48-year-old woman was admitted to the sanatorium on July 17, 1956, in a severely malnourished and depressed condition. The case history revealed that she had always been somewhat emotional and had had "migraine" headaches for years, which had been increasingly severe in recent years. They had been associated with nausea and vomiting, and in the past year there had been considerable weight loss and emotional depression. There had been several suicidal attempts during that period, and the headache had been constant. The patient was very thin and disturbed and complained constantly of headache, abdominal pain, and nausea. She received 12 electroshock treatments and was discharged Aug. 24, much improved. When last seen Oct. 18 she was quite well, had had no more headaches, and was making plans to return to work.

This case illustrates the development of chronic pain in a somewhat unstable individual with migraine which apparently set the pattern for her pain reaction.

Case 5.—A 58-year-old woman was seen May 26, 1955. She had had hemiplegia on the right in 1951, after which she had had some pain in her right arm which had become increasingly more severe and constant for eight months. In the two months before her admission to the hospital the pain had been intolerable, and when anyone touched the arm it hurt terribly and pain radiated through the hand and up the arm. She had become restless, tense, and somewhat depressed in the preceding four months. She had been subjected to considerable emotional stress since her stroke. She had had a few electroshock treatments in Paris three years before hospital admission because of a depressive reaction and had felt somewhat depressed for a year preceding admission. Her blood pressure was 190/100 mm. Hg. There was a residual hemiparesis on the right with hyperalgesia and hyperpathia on the right, especially in the upper extremity. Mentally she was quite restless, tense, and depressed.

She received eight electroshock treatments and was confined to a sanatorium from May 28 to June 21, 1955. She was greatly improved until April, 1956, when her arm began to ache more and insomnia developed. She was planning to go to Europe and was concerned about the problems she would have to face there. She appeared to be somewhat indecisive and depressed. She was given three outpatient electroshock treatments in April, 1956, and has remained quite well since.

This case illustrates the development of intolerance of chronic thalamic pain with increased emotional stress and depression, with relief with electroshock treatment.

Case 6.—A 62-year-old woman consulted me Dec. 22, 1954, complaining of pain in her legs ever since an accident eight years before in which she had fractured both legs. Her

husband had been killed in the accident, which upset the patient considerably. She was troubled so much by pain that the left kneecap had been fused in 1952. The pain was worse after the operation. The patient was unable to give a clear history of her pain. Apparently it was relieved by rest in bed, but when she went to bed at night it took her several hours to settle down and get to sleep. On awakening in the morning she felt free of pain, but after she got up and moved around the pain returned. She felt that the pain made her nervous and that the nervousness aggravated the pain. At times she became quite depressed, and her son stated they could not get her interested in anything outside her complaints. Early in her illness she had used alcohol for relief and at one time was drinking excessively. She stopped drinking after she fell and bumped her head.

Examination revealed no physical or neurological abnormalities except for a stiff knee joint on the left. She was somewhat depressed and at times had suicidal ideas. Symptomatic treatment gave no significant relief. Therefore, on July 12, 1955, outpatient electroshock treatment was started. This was given as needed for symptomatic relief, the patient having immediately responded favorably. On Oct. 22, after the 11th electroshock treatment, she was apparently free of leg pain. She was, however, quite tense and had considerable gastrointestinal distress. Because of this she was admitted to a sanatorium on Nov. 1, and her condition improved. Mild pain in the legs recurred, and she was given one more electroshock treatment. Subsequently she felt quite well and was discharged on Nov. 15, free of complaints.

She got along well until November, 1956, when, with onset of cold weather, her legs again began to ache and she felt some generalized fatigue and malaise. This persisted, and she was given an outpatient electroshock treatment on Jan. 14, 1957.

This case illustrates the development of chronic leg pain after injury. There was an associated emotional depression due to the death of the patient's husband in the same accident. Pain was increased by surgery performed for relief and was associated with increase in depression. After shock treatment the patient still had some pain on occasion but was able to tolerate it more satisfactorily. She, however, never improved to the point where she did not require sedation, especially when pain was troublesome.

Case 7.—A 46-year-old woman lacerated her left index finger on Sept. 27, 1955. The wound was repaired, but she developed considerable swelling of the finger. This swelling was mistakenly attributed to a bone infection. After a month, because of severe pain and swelling, she consulted another doctor who treated her for six weeks without benefit. The finger was then reexplored for a piece of glass. None was found, but a cut tendon not previously diagnosed was repaired. Subsequently the pain persisted, though the swelling subsided, and the patient developed the typical picture of causalgia, with redness and coldness of the finger, wasting and weakness of muscles of the hand, and pain which at times radiated up to the shoulder.

A stellate block gave considerable relief in March, 1956, so a left upper thoracic sympathectomy was done. Some relief of pain in the finger was obtained. However, the patient proved to be quite nervous postoperatively, was easily upset by hospital personnel, and at times was emotionally disturbed. She was discharged at her insistence. There was some improvement in circulation in the left hand, and the patient maintained some reduction of pain in the finger but complained bitterly of chest pain in the distribution of the second and third thoracic segments. This continued, and when she consulted me April 28, 1956, she was suffering a great deal of pain in the left arm and left part of the thorax. She was taking considerable medication, including codeine, and would take so much if unsupervised that her husband could no longer leave her home alone.

After admission to a sanatorium she wept a great deal and was depressed and complained constantly of pain, demanding something for relief. She was disturbed at night. At times she refused to wear the hospital gown on her left arm because it was so painful. She remained in bed constantly. She was given three electroshock treatments weekly for four weeks. At the time of discharge on May 29, 1956, she occasionally complained of moderate pain in the left shoulder, which was relieved by Bufferin (acetylsalicylic acid buffered with aluminum glycinate and magnesium carbonate). Otherwise she felt well and had been sleeping well.

She was brought to see me on July 7, 1956, by her husband, who stated that the patient had done well for several weeks after discharge and then, because of increasing pain, had consulted her family physician, who, instead of advising her to return, had given her the same medicament she had previously taken to excess. She was again complaining of constant pain in the left upper extremity and the left part of the chest and was somewhat agitated and depressed. She was given five outpatient electroshock treatments in July, after which she made a complete recovery. When last seen she was cheerful, optimistic, and was not concerned about a little distress over the left part of the thorax.

This case illustrates the development of chronic causalgic pain after an injury, pain increased by surgery and associated with considerable emotional disturbance and depression. After electroshock treatment there was still some discomfort in the patient's chest, but she tolerated this satisfactorily.

Case 8.—A 59-year-old man was referred to a neurology clinic Sept. 24, 1956, because of the complaint of persistent pain in an operative scar for hiatal hernia, which circled his chest on the left. The patient had had abdominal pain and vomiting for five years before May, 1955, when he underwent repair of a hiatal hernia, gastrectomy, and pyloroplasty. As a consequence of pain in his chest, he had an intercostal nerve block in January, 1956, excision of the sixth and seventh costal cartilages on the left in February, 1956, and neurectomy of the sixth and seventh thoracic sensory roots on the left with neurotripsy of the eighth thoracic root in April, 1956, all without benefit. In July, 1956, he shot himself in the left side of the chest, having become increasingly depressed because of the pain and his difficulty in obtaining satisfactory work. He recovered promptly from the gunshot wound but continued to complain of pain in the chest and required considerable medication for relief.

When the patient was seen by me, he did not appear to be seriously depressed. It was felt that the pain was probably largely psychogenic in nature and that before any further neurosurgical procedure was done he should be given procaine hydrochloride intravenously and, if this was not beneficial, electroshock therapy. The procaine gave no relief, so electroshock treatment was instituted. After eight treatments the patient felt much better and no longer required drugs for relief of pain. Improvement was maintained, and he was discharged in February, 1957. He still had some pain in the scar, but it no longer troubled him.

This case illustrates the development of chronic pain after surgery for relief of a condition causing intermittent pain. Subsequent surgery for relief of pain was ineffective, and suicide was attempted. The patient did not appear to be severely depressed and after two months of inpatient psychiatric treatment was referred to the neurology clinic for con-

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sideration of further treatment, possibly surgical. After electroshock therapy, he had some discomfort in the scar but it no longer bothered him.

Comment

The cases cited were chosen to illustrate some of the difficulties facing the clinician when he is confronted by a patient with chronic pain.[6] Often the patient has seen a number of physicians before and has had repeated examinations and many times surgery in the physician's attempt to diagnose or treat the condition. Too often the patient has become dependent on drugs, which further complicate the problem. While all the patients cited above received electroshock treatment, it should be emphasized that it is not my contention that this is the treatment of choice in such cases but that this represents an approach which can give good results in problem cases and that it should be considered at least before any neurosurgical procedure, such as frontal lobotomy or chordotomy is done. Under certain circumstances, especially where prolonged institutional care under psychiatric supervision is possible, satisfactory results can be obtained in some instances by psychotherapy.[7]

The explanation for the favorable results after electroshock treatment in the cases cited above is not yet entirely clear. According to the concept presented in this paper, chronic intolerable pain, regardless of specific cause, depends on reverberating circuits that are perpetuated by stimuli coming from the periphery, the cortex, or both. Electroshock therapy may produce its effect either by relief from the emotional depression, with resultant reduction in morbid preoccupation and anxiety, or from a reduction in the influence of the cortex on the reverberating circuits, or both, because of some modification in activity of the neuronal systems involved. It would seem that the same effect could be obtained, though more slowly, by psychotherapy and institutional care. The use of electroshock therapy in my opinion is more desirable in severe cases because of the rapidity with which both physical and emotional improvement can be obtained.

The criteria for selection of patients for this therapeutic approach are not well defined. Since cortical influences seem so significant in patients with chronic intolerable pain, it would appear that the prognosis is best for the condition of patients who are basically emotionally sound and developed their illness as a result of a painful experience or a series of painful experiences, in combination with emotional stress not necessarily related to the individual's illness. This would seem to be true especially where depressive elements are prominent and where the emotional conflicts may be resolved. It is my impression, however, that any patient with chronic intolerable pain not due primarily to some progressive disease such as carcinoma should be given a trial on electroshock treatment before frontal lobotomy is considered, particularly if measures to relieve the peripheral stimuli have been ineffective.

The use of electroshock therapy in the type of case cited here is not without difficulty. The period of treatment is often prolonged and several courses of electroshock treatment always combined with drug therapy and supportive psychotherapy may be necessary. The patient, the family, and the referring doctor usually have the concept that electroshock therapy is for the insane and resent its recommendation. Unless a complete understanding of the total situation can be obtained, the program is not advisable. Pentobarbital given orally one to two hours before treatment, with amobarbital sodium given intravenously in sufficient dosage to produce light sleep just before treatment, does much to allay the anxiety related to the procedure.

Summary

In five of eight cases of chronic intractable pain which had been unresponsive to medical or surgical treatment, surgical measures for relief of primary cause of pain were ineffective and generally seemed to make the condition worse. It is believed that chronic pain is the product of reverberating circuits in the nervous system, of which the cortical components are of great importance. Electroshock therapy gave marked benefit or relief from pain in all cases reported. Thus, this represents one approach to the treatment of chronic pain which should be tried in many instances before such patients are subjected to some neurosurgical procedure, particularly lobotomy, for relief of pain or abandoned to drug addiction.

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A PRESSOR PHENOMENON ASSOCIATED WITH THE POSTPARTUM PERIOD

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Of 23,600 patients who delivered during the past four years, 2,311 patients had to be followed in a toxemia clinic. Serial studies on these patients revealed that 464 (20%) showed the highest level of arterial pressure during the 3-to-17-week postpartum period. In 133 of these patients this respresented the first appearance of hypertension. Their history, pregnancy, delivery, and immediate postpartum period were entirely normal. In 331 patients there was a history of prior hypertension. It would seem from these studies that a previously unrecognized pressor phenomenon, practically confined to multiparas, was active during the postpartum period. Since the condition is self-limited, therapy by drugs, restriction of activity, or diet is not indicated. The possibility of a relationship to a vascular disease later in life remains to be studied.

Previous publications from this clinic have been concerned with pyelonephritis and hypertensive vascular disease masquerading as toxemia of pregnancy and the frequency of hypertensive disease in the young pregnant female.[1] More recently our interest has centered around a group of asymptomatic patients with an entirely normal history, pregnancy, delivery, and immediate postpartum course, with the first occurrence of an elevated blood pressure reading occurring two to seven weeks post partum. Although the syndrome of postpartum hypertension has been recognized by Stout,[2] Meyer and Nadler,[3] and Dieckmann [4] as not uncommon, its frequency has not been appreciated by obstetricians or internists.

The frequent finding of the highest level of arterial pressure in patients with chronic hypertension (history of hypertension prior to pregnancy) occurring during the period from 2 to 20 weeks post partum stimulated our interest further and suggested the possibility that some type of pressor mechanism might be operative then. Many questions have arisen. What types of patients develop postpartum hypertension? Is there a relationship between parity and age and the development of hypertension? What factors initiate the pressor phase? What causes its termination? Are there any clues to the underlying pathogenesis? Is there a relationship between postpartum hypertension and the development of chronic hypertensive vascular disease?

During the past four years there have been 23,600 deliveries at the District of Columbia General Hospital (fig. 1). Less than one-half of these patients returned to the postpartum clinic. Of these 10,002 patients, 7,691 were entirely normal (showing no evidence of cardiovascular-renal disease) and were immediately discharged by the obstetricians. The remaining 2,311 of these patients showed evidence or history of an elevated blood pressure, edema, or albuminuria and were referred to the toxemia clinic. Four hundred sixty-four patients showed the highest level of arterial pressure during the postpartum period. One hundred thirty-three of these patients were given a diagnosis of postpartum hypertension, and 331 were patients with a history of hypertension prior to pregnancy. An analysis of these two groups of patients is the subject of the present report.

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Read in part before the national meeting of the American Federation for Clinical Research, Atlantic City, N. J., May, 1957.

Methods and Materials

Patients were not included in this study if complete antenatal and hospital records were not available. Any history of hypertension or renal disease prior to pregnancy, or any cardiovascular-renal abnormality during pregnancy or delivery (even a trace of edema or albuminuria), or any abnormal physical finding in addition to the elevated blood pressure reading excluded the diagnosis of postpartum hypertension. The patients with chronic hypertensive vascular disease were also followed in the toxemia clinic during their antenatal course.

Besides the usual obstetric examination, a complete cardiovascular examination was performed in both groups, including careful ophthalmoscopic examination and urinalysis. During the postpartum period the patients were examined at two-week intervals until the blood pressure had returned to its usual level. Ten patients who were given a diagnosis of postpartum hypertension were hospitalized to determine the result of 72 hours of bed rest on the arterial pressure. An electrocardiogram, x-ray of the chest, and urine culture were performed on each. After the period of bed rest, the responses of the arterial pressure to 5 mg. of phentolamine

methanesulfonate given intravenously, to 0.05 mg. of histamine base given intravenously, and to the head-up tilt position were tested.

Results

Group with Postpartum Hypertension.—One hundred thirty-three patients had postpartum hypertension; they represented 1% of the 10,002 patients who returned to the postpartum clinic during the

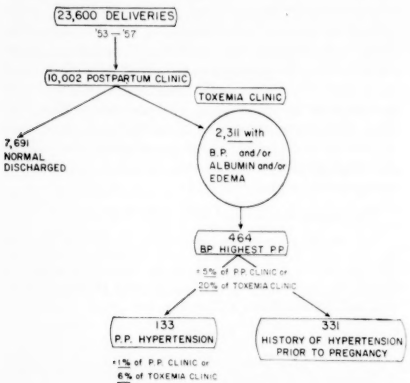

Fig. 1.—Distribution of patients with postpartum hypertension at District of Columbia General Hospital.

past four years and 6% of the 2,311 patients followed in the toxemia clinic. Their average age was 28 years (14 to 44). Multiparity predominated; the average number of children was 5 (1 to 14). The average time for the first appearance of the hypertension was three weeks (two to six weeks). The highest level of arterial pressure was most frequently recorded at 6 weeks (5 to 8 weeks); and the average duration of the postpartum hypertension period was 17 weeks (6 to 11 months). The mean arterial pressure rose from an average of 92 ± 10 mm. Hg to 127 ± 13 mm. Hg, a 38% average increase.

In the patients hospitalized, 72 hours of bed rest was associated with a 13% average reduction in arterial pressure (127 ± 13 mm. Hg to 110 ± 9 mm. Hg). There was no abnormality in the electrocardiogram or chest x-ray of any patient. Similarly, the blood pressure response to phentolamine, histamine, and tilting was not abnormal.

Group with Chronic Hypertension.—In the past four years, 1,130 patients with a history of hypertension prior to pregnancy have been followed in the toxemia clinic. Three hundred thirty-one, or 29%, of these patients have consistently shown the highest level of arterial pressure during this period from 2 to 17 weeks post partum. Their average age was 29 (13 to 43). Again multiparity predominated, with an average of 5 children per patient (1 to 14). The average time of the first appearance of an elevated arterial pressure above the usual hypertensive level was 3 weeks post partum (4 to 10 weeks); and the average duration of this hypertensive state was 9 weeks (15 to 28 weeks). The mean arterial pressure increased from an average of 124 ± 17 mm. Hg during pregnancy to 142 ± 17 mm. Hg, a 15% average increase.

Comment

Although the syndrome of postpartum hypertension is rare, occurring in 1% of normal postpartum patients, it would seem that the presence of a pressor phenomenon during the postpartum period is rather common (fig. 1). In addition to the 133 patients with postpartum hypertension, there were 331 patients with a history of hypertension prior to pregnancy who showed the highest level of arterial pressure during the postpartum period. This total of 464 patients represents 5% of the total postpartum population or 20% of the toxemia clinic. In other words, 20% of the patients who exhibited any pressor phenomenon in relation to pregnancy showed the highest level of arterial pressure during the postpartum period.

Further evidence for the existence of a pressor phenomenon during the postpartum period can be gained from serial studies on 30 patients followed through three pregnancies (fig. 2). The only elevations of arterial pressure in these patients occurred during the postpartum period. Four of the latter group are now being treated in the hypertensive clinic for persistent hypertension. In these four patients, it would seem that postpartum hypertension was the forerunner of hypertensive vascular disease. Whether long-term follow-up studies on the other patients will show that hypertensive vascular disease is a common outcome of postpartum hypertension is not known.

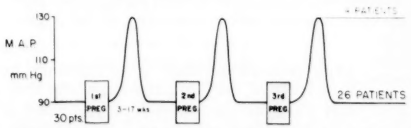

Fig. 2.—Studies of 30 patients followed through three pregnancies.

The cause of the pressor phenomenon in both of these groups is unknown. Preliminary pressor and depressor studies have not given a clue as to the underlying etiology in the postpartum hypertensive group. It does not seem to be due solely to anxiety, nor does it seem to represent merely a labile blood pressure in a tense patient, since the arterial pressure in these patients was not significantly elevated

during labor or delivery, usual times of stress and anxiety. The lack of a drastic reduction in blood pressure after bed rest would also tend to minimize anxiety as playing an important role in the production of this type of hypertension. Since these patients have not been completely evaluated psychoanalytically, the role of subconscious anxiety and frustration in the pathogenesis in this syndrome cannot be completely evaluated.

Whether there is a relationship to multiparity is uncertain, although it would seem from our studies and from the studies of others [5] that this transitory postpartum hypertension is seen almost exclusively in multiparous women. Our data are also in agreement with those of Stout [2] and Meyer and Nadler,[3] who found postpartum hypertension in an older obstetric age group. Although the average age of the patients with postpartum hypertension reported here is only 29, the average age of our clinic population taken as a whole is 24. This latter observation would seem to be in keeping with the earlier appearance of hypertensive disease in Negro women as reported by Schulze and Schwab [6] and one of us.[1b]

In order that the natural course of the disease might be studied, patients with postpartum hypertension purposely have not been given any type of therapy. Whether therapy might shorten the duration of the hypertensive period or prevent the development of persistent hypertension (if this is found to follow) is unknown. Since these patients are asymptomatic and without evidence of vascular disease except for an elevated arterial pressure, the only logical reason for treatment would be prevention of permanent hypertension. Studies are now in progress to determine to what type of hypotensive treatment these patients are most sensitive.

Since this is a self-limited state, one would have great difficulty in evaluating the effectiveness of any type of therapy since a fall in arterial pressure to normotensive levels might simply represent the self-termination of the hypertensive state. Until such studies can prove either shortening of the hypertensive period or actual prevention of permanent hypertension, no definitive hypotensive therapy or restriction of activity or diet would seem to be indicated.

Summary

The syndrome of postpartum hypertension, that is, an asymptomatic elevation of arterial pressure 2 to 17 weeks post partum in a patient with normal history, and normal pregnancy, delivery, and immediate postpartum period, is rare, occurring in 1% of normal postpartum patients or 6% of our toxemia clinic population. The pressor phenomenon associated with the postpartum period is rather common, however, since, in addition to the patients with postpartum hypertension, 331 patients with a history of hypertension prior to pregnancy, or a total of 20% of our toxemia clinic population, showed the highest level of arterial pressure during the postpartum period.

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Drug Evaluation.—There is no substitute for adequate clinical pharmacology plus a sound knowledge of the characteristics of the drug under test. When this has been done, then, and only then, can we approach an evaluation of the psychogenic responses unrelated to the specific drug effect as compared to the specific drug response. It is becoming increasingly difficult to separate nonspecific psychosomatic drug responses from specific drug effects in the evaluation of drugs that affect the central nervous system, particularly those used for treating psychiatric conditions. Under these circumstances, specific responses to drugs fade progressively into nonspecific psychological effects. The evaluation of this grey zone presents difficulties, chiefly because of the lack of objective tests for evaluating drugs in mental and emotional disturbances. When the use of subjective criteria is essential, placebo substitution is a requirement for evaluating therapeutic agents. If the range between maximum therapeutic effect and intolerable side-reactions is sufficiently wide, double-blind procedures may be the method of choice for evaluating therapeutic efficacy of drugs used for specific disease entities.—J. H. Moyer, The Psychosomatic Problem in Drug Evaluation, *A. M. A. Archives of Internal Medicine,* November, 1956.

OPEN HEART SURGERY

ANESTHESIA AND SURGICAL EXPERIENCES

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Open heart surgery under direct vision is now performed by using either hypothermia or extracorporeal circulation. The latter method, in which circulation is completely diverted from heart and lungs by using a pump-oxygenator, was used in 53 operations. Thirty of these were for the correction of aortic stenosis, and extracorporeal bypass times up to 85 minutes were found to be compatible with survival. Details of anesthesia, surgical procedure, and record-keeping are given. The tetralogy of Fallot was corrected in four patients, with zero mortality. Eight of the 14 deaths in other cases resulted from ventricular fibrillation with or without complete heart block. Open heart surgery at present has definite advantages and disadvantages. The latter are such that curative surgery by closed techniques, when feasible, will continue for some time to have a higher survival rate.

Open heart surgery for the complete correction of congenital and acquired cardiac lesions is now feasible in certain well-selected instances. In 1939 Gibbon reported the first successful bypass of the heart and lungs in a living patient.[1] The stimulus to undertake operations within the heart was sparked by his work. In June, 1948, the first successful instance of effective (closed) intracardiac valve surgery was reported by one of us.[2]

At present there are two distinctly different methods by which open heart surgery can be accomplished under direct vision. These are hypothermia (a reduction of body temperature) and extracorporeal circulation by use of the heart-lung (pump-oxygenator) apparatus. Each of the two techniques has distinct advantages over the other. It is contrariwise true that the disadvantages of each are prominent. Neither fully encompasses the ideal essentials of (1) rapid application and unconstrained use, (2) a completely bloodless field in which to work, (3) maintenance of normal physiology of the entire organism, (4) avoidance of air embolization, (5) preservation of the coagulability of the blood, (6) freedom from major conduction discrepancies of the heart, and (7) a heart that will spontaneously assume and sustain normal action when reverted into the systemic circulation.

Hypothermia

Hypothermia can be achieved rapidly by anesthetizing the patient to the second or the third plane of third-stage anesthesia and then immersing the patient in a container of cold solution, as advocated by Swan and Virtue.[3] In the past we have usually preferred the more deliberate and controllable reduction of body temperature by mattress cooling.[4] Recently, a modified Blades [5] technique has added to the adaptability of hypothermia in achieving open cardiotomy for atrial septal defects. The diagnosis of ostium primum defects is most accurately made after atriotomy on the right side of the heart and exploration of the septum. It has been our belief and practice that atrioseptopexy for ostium secundum defects by the closed technique is less hazardous to the patient, equally effective, and more rapidly accomplished. However, satisfactory closure of the ostium primum defects by the closed technique has not been dependable or always possible. Thus, closure has sometimes required open cardiotomy. Blades has recommended the circulation of a sterile cooling solution within the closed thorax. We have adapted the instillation of cold saline solution into the right open hemithorax and removal of the saline solution from the left side of the chest. It is possible thereby to observe directly the cardiac action during cooling and to reduce the body temperature from 98.6 F (37 C) to 85 F (29.5 C) within one and one-half to two hours in an adult.

The advantages of hypothermia are as follows: 1. It affords a means of accomplishing open cardiotomy for periods of time up to 15 minutes, with the body temperature reduced to 85 F. 2. The patient need not be heparinized. 3. The method can be executed with a minimal amount of equipment and personnel. 4. It reduces the oxygen requirements of the entire organism.

The disadvantages of hypothermia are as follows: 1. It produces alterations in the conduction mechanism within the heart. 2. It predisposes to shivering.

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3. It predisposes to ventricular fibrillation. 4. It allows only a brief period of time for definitive surgery (15 minutes or less) while the heart is open.

Extracorporeal Circulation

Various investigators have proved that it is possible to bypass the right side of the heart,[6] to bypass the left side of the heart,[7] and to completely bypass the heart and lungs.[8] The most widely accepted

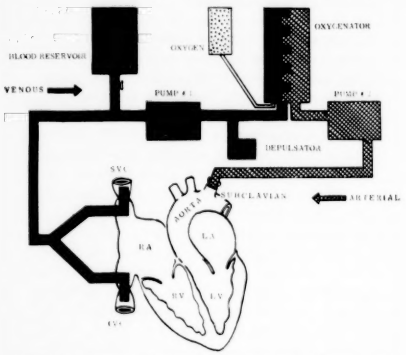

Fig. 1.—Diagram of open heart surgery with bypass technique in which circulation is diverted from heart and both lungs.

method of open cardiac surgery with the bypass technique has been to exclude the heart and both lungs from the systemic circulation during the time utilized for definitive surgery (fig. 1).

The advantages of using a pump-oxygenator are as follows: 1. The circulation can be diverted from the heart for at least 85 minutes (our longest period). 2. The surgery can be done in a relatively bloodless, quiet field. 3. More than one defect can be corrected during a single operation, i. e., ventricular septal defect and associated pulmonary stenosis.

The disadvantages of extracorporeal circulation are as follows: 1. Mechanical deficiencies of the pump, tubing, and/or oxygenator exist. 2. The patient must be heparinized. 3. Hemorrhage may occur during and after surgery. 4. There is a greater incidence of infection and septicemia. 5. Patients must be anesthetized for a considerable period of time prior to receiving benefit or correction of existing pathology. 6. Conduction defects are frequently major complicating factors, i. e., heart block and ventricular fibrillation.

We believe that, when extracorporeal circulation is to be used, the "heart-lung team" must consist of 15 well-qualified specialists. There are two anesthesiologists, four surgeons, two physiologists (to assimilate and disseminate information from the monitoring equipment), two individuals to control the pump-oxygenator, two suture nurses, two circulating nurses, and one hematology technician. It is, therefore, quite apparent that only in large medical centers, with ready access to such a large number of capable personnel, can open cardiotomy, utilizing extracorporeal circulation, be accomplished with acceptable results. The future will certainly bring refinements to both monitoring devices and the pump-oxygenator, so that fewer key members of the team will be required.

Types of Equipment

A variety of extracorporeal oxygenator systems are in general use for open heart surgery. The bubble method and the screen or rotating-disk type of systems currently are enjoying the most popularity and have had the widest clinical trial. These are all essentially filming types. The bubble method films the blood on the bubbles of oxygen introduced

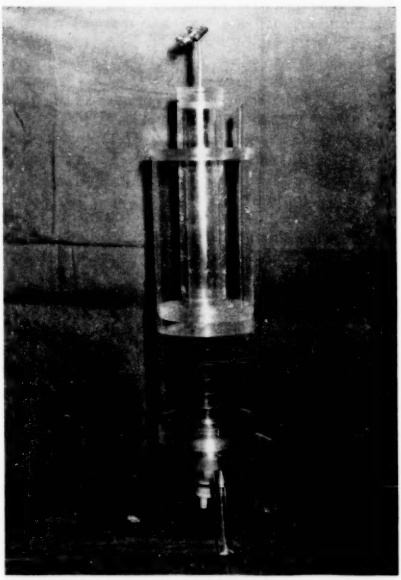

Fig. 2.—Bubble-type oxygenator made of nylon and acrylic plastic.

directly into the blood, whereas the screen or rotating-disk oxygenators film the blood in thin layers within an atmosphere of oxygen.

Homologous lungs and the semipermeable membrane have had some clinical application but not sufficient to permit a fair evaluation of the methods.[9] More recently, the use of the animals' own lungs

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has been undergoing experimental study. This is a promising method and should be more physiological than the artificial methods of oxygenation. Gollan, Blos, and Schuman have utilized hypothermia in conjunction with an extracorporeal oxygenator system.[10] The laboratory results suggest that the method has considerable merit for clinical application.

motor pump. The oxygenator, with the exception of the outer column, is made of nylon and is best sterilized by the autoclave. The outer column of heavy acrylic plastic is sterilized by boiling. This is an important consideration, as the danger of subacute bacterial endocarditis, particularly in aortic stenosis, is great if cold sterilization with benzalkonium (Zephiran) chloride solution is utilized. We have had five cases of septicemia due to Pseudomonas aeruginosa, all of which proved fatal, when cold sterilization was used for the oxygenator. Since the mode of sterilization was changed there has been no subsequent infection due to Pseudomonas organisms.

TABLE 1.—*Data on Fifty-three Patients on Whom Open Heart Surgery Was Performed*

Case No.	Age, Yr.	Weight, Lb.	Weight, Kg.	Diagnosis	Duration of Anesthesia, Hr., Min.	Extracorporeal Time, Min.	Blood Replacement	
							Citrated, Ml.	Heparinized, Ml.
1	6 mo.	14	6	Ventricular septal defect	4, 30	20	20	250
2	15	92	42	Tetralogy of Fallot	6, 30	56	3,000	9,000
3	14	120	54	Aortic stenosis	7, 0	10	1,000	500
4	21	172	78	Aortic stenosis	6, 15	17	650	3,000
5	5	30	14	Ventricular septal defect	6, 0	31	400	725
6	58	158	72	Aortic stenosis	4, 15	11	1,500	1,000
7	31	158	72	Aortic stenosis	6, 0	15	2,500	2,800
8	36	154	70	Aortic stenosis	5, 0	22	1,500	2,500
9	32	124	56	Atrioseptal defect	5, 0	3	1,250	3,450
10	14	152	69	Aortic stenosis	6, 0	11	1,500	4,250
11	37	122	55	Aortic stenosis	6, 30	12	2,000	3,500
12	15	113	51	Tetralogy of Fallot	7, 0	31	2,000	1,750
13	55	165	75	Aortic stenosis	5, 30	15	1,500	2,500
14	37	172	78	Aortic stenosis	7, 0	12	2,000	2,000
15	18	156	71	Ventricular septal defect	5, 30	14	1,000	2,000
16	45	134	61	Aortic stenosis	7, 0	15	2,500	1,500
17	38	114	52	Aortic stenosis	6, 0	11	2,500	1,500
18	44	163	74	Aortic insufficiency	6, 0	85	1,500	2,500
19	44	168	76	Aortic stenosis	6, 15	19	1,000	1,500
20	3 mo.	10	4	Transposition of great vessels	6, 0	13	300	1,500
21	19	110	50	Aortic stenosis	5, 0	33	1,500	1,000
22	7 mo.	13	6	Ventricular septal defect	5, 0	74	100	850
23	52	148	67	Aortic stenosis	5, 0	24	1,000	3,350
24	42	135	61	Mitral insufficiency	5, 30	10	1,500	1,800
25	33	121	55	Aortic stenosis	3, 30	25	1,000	2,600
26	43	191	87	Aortic stenosis	4, 30	21	1,300	1,800
27	59	139	63	Aortic stenosis	4, 30	11	1,100	2,500
28	50	161	73	Aortic stenosis	3, 30	14	500	1,500
29	52	150	68	Aortic stenosis	5, 30	14	1,500	2,500
30	52	161	73	Aortic stenosis	6, 15	30	2,500	4,250
31	49	152	69	Aortic stenosis	5, 30	20	2,000	3,750
32	43	168	76	Aortic stenosis	5, 30	9	3,000	3,000
33	1 mo.	6	3	Transposition of great vessels	5, 30	27	85	900
34	32	136	62	Aortic insufficiency	5, 30	26	3,000	1,350
35	25	90	41	Mitral insufficiency	4, 45	26	600	4,500
36	41	132	60	Mitral insufficiency	5, 30	21	1,500	2,500
37	44	158	72	Aortic stenosis	7, 15	15	1,500	2,500
38	31	152	69	Mitral insufficiency	5, 30	26	2,000	5,500
39	43	172	78	Aortic insufficiency	4, 15	26		2,000
40	3	27	12	Tetralogy of Fallot	4, 30	30	200	900
41	58	161	73	Aortic stenosis	5, 15	11	1,125	2,225
42	16	105	48	Ventricular septal defect	5, 0	32	1,500	3,300
43	46	92	42	Aortic stenosis	6, 15	9	2,000	2,000
44	63	158	72	Aortic stenosis	6, 15	16	3,000	3,200
45	10 mo.	12	5	Ventricular septal defect	5, 15	50	215	950
46	7	41	19	Tetralogy of Fallot	5, 0	42	525	2,575
47	9	51	23	Ventricular septal defect	5, 0	30	450	1,500
48	53	144	65	Aortic stenosis	4, 45	36	2,000	3,000
49	55	121	55	Aortic stenosis	6, 0	28	2,000	4,250
50	42	126	57	Aortic stenosis	5, 30	37	2,500	2,000
51	37	163	74	Aortic insufficiency	5, 15	60	1,100	3,000
52	51	151	68	Aortic stenosis	4, 0	37	1,000	3,000
53	9	48	22	Ventricular septal defect	4, 45	50	500	1,000
Averages	32.6	125.4	54.8		5, 30	26	1,400	2,450

The equipment used in our experience is a bubble-type oxygenator, designed by Gilman and Gemeinhardt.[11] It is a vertical column made of nylon and acrylic plastic, with the bubbling tube, defoaming chamber, and reservoir combined in a single unit (fig. 2). The blood is moved by the use of a Sigma-

Selection of Cases

We have performed 53 operations in which the circulation has been completely diverted from the heart and lungs. The existent pathology was as follows: ventricular septal defects, 8; ventricular septal defects and pulmonary stenosis (tetralogy of Fallot), 4; transposition of great vessels, 2; atrial septal defects, 1; aortic stenosis, 30; aortic insufficiency, 4; and mitral insufficiency, 4.

According to table 1, the variations in age of the patients were from 1 month to 63 years of age, with 32.6 years as the average. The weight variations were from 6 lb. (2.7 kg.) to 191 lb. (86.6 kg.), with 125.4 lb. (57 kg.) as the average. The duration of anesthesia varied from the shortest period of 3 hours and 30 minutes to the longest of 7 hours and 15 minutes, with 5 hours and 30 minutes as the average period of anesthesia. Extracorporeal bypass times were as short as 3 minutes in one case and as long as 85 minutes in the longest case, with 26 minutes as the average in the 53 cases.

Anesthesia Management

Meperidine (Demerol) hydrochloride has been used in conjunction with atropine sulfate for preliminary medication in all patients with congenital heart disease. The usual dosage of meperidine hydrochloride administered has been 1 mg. per pound of body weight, but it has not exceeded 100 mg. in any patient. Infants and small children, who were judged by the anesthesiologist to be inadequately sedated when brought to the operating room, have received 6 to 10 mg. of thiopental sodium administered intramuscularly for each pound of body weight. Preliminary medication in the group with acquired heart disease has consisted of the oral ingestion of a short-acting barbiturate 90 minutes prior to the induction of anesthesia; atropine sulfate has been administered by hypodermic injection 30 minutes later.

All anesthesia equipment and supplies that may be used during the anesthetization period have been prepared and placed in a readily available location. The patients are carefully surveyed in the operating room, prior to induction, for evidence of hypotension, tachycardia, fever, or any evidence of heart failure. Venous cannulas, previously placed, are rechecked to ascertain patency.

The trachea is intubated under direct vision. The largest caliber catheter that can be introduced without trauma is inserted. Infants and children are especially prone to develop laryngeal edema from trauma or pressure. Because of this fact, tubes without cuffs are utilized if the patient is less than 12 years of age.

Respirations are controlled from the time of intubation until the chest walls have been made airtight after closure, and no evidence of pneumothorax in either hemithorax exists. Voluntary respirations rapidly return, but may require assistance by the anesthesiologist for 10 to 15 minutes before becoming adequate. The major physiological changes, prior to cannulation of the arterial and venous system, occur from bilateral pneumothoraxes and the depressant effect of prolonged anesthesia in cardiac patients. Each patient has received 1.5 mg. of heparin intravenously for each kilogram of body weight. The patient is heparinized for 5 to 10 minutes prior to the insertion of the cannulas.

The venae cavae are isolated, and umbilical tapes are passed around them at their entrance site into the right atrium. One of the subclavian arteries is isolated and cannulated. The coronary sinus may be cannulated if the operation is to be performed for aortic valvular disease. The coronary sinus is catheterized, prior to open cardiotomy, by a closed technique. The cavae are catheterized via either the right auricular appendage or the right atrial wall. The catheterization of the cavae should be last, as it causes partial obstruction of the cavae. This obstruction increases the venous pressure and reduces cardiac output, while the heart continues to maintain the circulation.

Immediately after complete arterial and venous cannulation the pump-oxygenator is started, and the patient placed on partial bypass. This phase of partial bypass affords the opportunity to determine the patency of cannulas and to ascertain that the mechanical apparatus is in correct working order. If the apparatus is found to be in proper functioning order, the umbilical tapes are secured tightly around the cavae. This maneuver excludes the heart from the circulation except for the coronary flow, and the patient is on total bypass.

At our clinic the flow rate is not predetermined by body size alone but is established principally by the venous return to the oxygenator. The venous return is increased to the maximal obtainable flow, and the arterial flow is brought into exact balance. If the blood volume is deficient, the oxygenated blood in the arterial reservoir will be quickly depleted when precalculated flow rates are used. With our present technique it is possible to keep in proper blood volume balance and to detect quickly inadvertent venous catheter obstruction.

Retrograde coronary sinus perfusion is started in most patients with aortic valvular disease after the aorta has been cross clamped and opened. The flow of the coronary sinus perfusion is regulated, so that only a small amount of unoxygenated blood may be observed coming out of the coronary artery ostiums. A high flow not only will cause the field to be obscured by blood but also, we believe, has a deleterious effect because of the congestion of the delicate capillary network of the ventricular myocardium. The usual flow into the coronary sinus perfusion varies from 75 to 200 ml. per minute.

Total bypass is maintained with flow rates of 50 to 80 ml. per kilogram of body weight. The body chemistry has been kept within reasonable limits

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during these procedures, and destruction of the blood elements has been minimal (table 2). During total bypass the mean blood pressure has been maintained with the Sigmamotor pump between 60 and 70 mm. Hg. After completion of the definitive intracardiac surgery and closure of the cardiotomy wound, the perfusion flow rate is reduced by approximately one-third. The tourniquets are removed from around the cavae, and the heart is allowed to resume normal function.

Manual compression of the breathing bag may be carried out by the anesthesiologist during open cardiotomy in order to maintain a quiet mediastinum. Severe diaphragmatic contractions are best controlled by constant administration of succinylcholine chloride. No anesthetic gas, other than oxygen, has been required after total bypass. The patients, who are lightly anesthetized, frequently will obey spoken commands (i. e., to open or close their eyes), but they have no memory of being awake or complaints related to pain.

Once spontaneous cardiac action has been obtained, the cannulas are removed from the right atrium to allow better filling. The arterial cannula is removed last, and a heparin neutralizing agent is injected intravenously. We have used both protamine sulfate and hexadimethrine bromide (Polybrene), which is a quaternary ammonium salt and a linear polymer, for deheparinization. We prefer hexadimethrine bromide because of its more predictable action in prolonged neutralization of heparin.[12]

We have found that the body temperature is reduced in all cases in which the heart and lungs are excluded from the circulation, unless a warming mechanism is incorporated with the bypass apparatus. The temperature is reduced in direct proportion to the length of time of total bypass and inversely to the size of the patient.

TABLE 2.—*Laboratory Data on Seventeen Patients Who Had Total Cardiopulmonary Bypass*

Case No.	Oxygen Saturation, %	pH	Hemolysis, %	Hemoglobin, Gm./100 Cc.	Hematocrit, %	White Blood Cells, per Cu. Mm.	Platelets, per Cu. Mm.	Carbon Dioxide, Vol. %	Lactic Acid, Mg./100 Cc.
				Before Perfusion					
1	95.3	7.39		11.2	39	8,500	140,000		
2	100	7.42		15.2	47	7,600	150,000		
3	100			12.6	37	14,700	240,000		
4	100								
5	71.9			17.3	55	13,850	130,000		
6	100			15.4	47	10,300	310,000		
7	100	7.37		15.4	49	11,500	170,000		
8	100	7.39		15.2	46	11,400	260,000		56
9	100	7.41		13.4	42	12,950	360,000		71
10	100	7.40						33.8	
11	100	7.39		14.5	45	11,000	210,000		101
12	100	7.40		14.4	43	6,250	370,000	38.9	56
13	100			13	40	9,500	180,000	35.3	72.5
14	100			17.7	46	7,950	120,000	31.9	85
15	100							31.4	62
16	100	7.39		15	47	10,250	320,000	32.9	59
17	100							43.1	59
				After Perfusion					
1	100	7.39		8.8	30	4,100	150,000		
2	96.4	7.48	7.9	13.2	42	8,800	180,000		
3	100		3	13.6	41	12,950	160,000		
4	100								
5	100			16	50	11,650	110,000		
6	100			14	44	9,500	270,000		
7	100	7.39	12.6	14.2	44	10,450	150,000		
8	100	7.37	15.5	13.4	41	8,000	200,000		91
9	100	7.36	13.2	11.2	35	8,900	240,000		126
10	100	7.37	13.8						
11	100	7.40	17.7	13.4	40	9,200	70,000		138
12	100	7.40	18.3	12	36	7,850	410,000		240
13	100		17.2	11.2	36	8,500	140,000		159
14	100		21	15.6	40	6,000	120,000		85
15	100		16.6						103
16	93.3	7.37			41	7,050	250,000		112
17	97.8			21					112

The assimilation and recording of data are difficult. We have therefore devised a standard form that has proved useful and adaptable for chronological recordings. We believe that universally well-kept records will aid all of us in establishing the proper indications and contraindications for extracorporeal circulation (table 3).

Results

The operative mortality is directly related in each case to the nature of the pathological defect or problem and to the severity of the clinical condition of the patient. Thus, the mortality encountered

in the correction of septal defects and in the tetralogy of Fallot has been zero, while that in complete transposition of the great arteries has been 100%. Certain inherent hazards and risks specifically related to the development and early utilization of the extracorporeal perfusion apparatus are apparent in any consideration of the immediate causes of death, as shown in table 4.

Conclusions

During the developmental stages of the application of the method of total cardiopulmonary bypass, the operative mortality has been high but not prohibitive. At the present time it is felt that certain inherent technical and mechanical difficulties which attend its use are sufficiently serious to preclude its general utilization for those lesions which may be treated effectively by existing closed techniques. It is obvious that such restriction of its use to the more severe types of cardiac deformation must ensure a continuation of high attendant risks and mortality.

As the various "bugs" are progressively diminished and eliminated, the more widespread, elective application of open cardiotomy in many less threatening conditions may be countenanced. However, we believe that curative surgery by the closed techniques, when feasible, has, and will continue to have, a higher survival rate. Open cardiotomy with direct-vision surgery is feasible and indicated at the present time in ventricular septal defects, in the tetralogy of Fallot, and in severe cases of aortic stenosis. The use of the extracorporeal circulation method represents the difference between palliation and cure in most of these conditions.

TABLE 3.—*Data Sheet Regarding Extracorporeal Circulation Method in Open Heart Surgery*

No..... Date.....
Name..... Age..... Weight.....Lb.....Kg.
Diagnosis..... Operation.....
Preoperative Data:
Lee & White coagulation time.....min.....sec.
Prothrombin time.....%
Hemoglobin.....Gm./100 cc. Hematocrit.....%
Oxygen saturation.....
Shunt or pressure gradient (liters/min.).....mm. Hg
Digitalized..... ECG.....
Temperature.....F Blood pressure..... Pulse.....
Preoperative Blood Volume:
Total plasma volume.....cc./kg. (35-45).....cc./sq. m. (1,300-1,700)
Total packed
red blood cells.....cc./kg. (30-40).....cc./sq. m. (1,150-1,550)
Total blood volume.....cc./kg. (65-85).....cc./sq. m. (2,500-3,200)
Start of Anesthesia.....
Anesthetics and amounts.....
Techniques .....
Lee & White time.....
Platelets ....
Start of Surgery.....
Amount of citrated blood prior to heparinization.....cc.
Heparin dose.....amount.....mg. I.V. (1.5 mg./kg.)
15-min. postheparin studies
Lee & White.....min.....sec.
Platelets ....
Hemoglobin.....Gm./100 cc. Hematocrit.....%
Carbon dioxide content.....mEq. Oxygen saturation.....%
Total Bypass Time.....min.....sec. Flow Rate.....cc./min.
Oxygen saturation during bypass.....%
Amount of heparinized blood.....cc.
Antiheparin agent..... dosage.....
Hexadimethrine, 1.5 mg./kg.
or
Protamine, 1.5 mg./kg.
Hypotension during subsequent 30 min.....
Oxygen saturation after bypass.....%.....min.
Fifteen-Minute Postheparin Neutralization Studies
Lee & White.....min.. .....sec. Platelets.....
Hemoglobin.....Gm./100 cc. Hematocrit.....%
Prothrombin.....% Carbon dioxide content.....mEq.
Amount of Citrated Blood After Neutralization.....cc.
End of Surgery..... End of Anesthesia.....
Postoperative temperature.....F
Complications During Anesthesia

Bradyeardia	Tachyeardia .....
Hypotension	Hypertension .....
Heart block	Ventricular fibrillation .....
Pulmonary edema	Hemorrhage .....
Caval obstruction	Mechanical .....

Postoperative Blood Volume:
Total plasma volume.....cc./kg. (35-45).....cc./sq. m. (1,300-1,700)
Total packed
red blood cells.....cc./kg. (30-40).....cc./sq. m. (1,150-1,550)
Total blood volume.....cc./kg. (65-85).....cc./sq. m. (2,500-3,200)
Two-Hour Postoperative Blood Studies
Lee & White.....min.....sec. Platelets.....
Hemoglobin.....Gm./100 cc. Hematocrit.....%
Prothrombin time.....% Carbon dioxide content.....mEq.

TABLE 4.—*Causes of Death During Anesthesia and Surgery*

Ventricular fibrillation	6
Ventricular fibrillation and complete heart block.....	2
Air embolization of coronary arteries.....	1
Pulmonary edema	4
Hemorrhage	1
Total.....	14

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CARDIAC REHABILITATION

QUESTIONNAIRE SURVEY OF MEDICAL DIRECTORS IN INDUSTRY

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Data obtained from 19 industrial organizations and representing 251,480 workers showed that nine organizations had hired cardiac patients during the past year. Among 19,321 new employees there were 242 with cardiovascular disease, including 53 classified as rheumatic and 24 as arteriosclerotic. All of the 19 organizations reported that it was their policy to return an employee to his job after recovery from an acute cardiac episode. The total number of deaths attributable to cardiovascular disease was 181 in an employee population of almost 170,000 and only 13% of these deaths occurred at work while 87% occurred off the job. Absenteeism is not a major problem among cardiacs; the major reason cited by industries reluctant to hire cardiacs is the threat of monetary loss from compensation claims, sickness benefits, or pension benefits. There is a need for more facts regarding the work experience of cardiac patients and the impact of workmen's compensation legislation upon employment policies; it will also be necessary to educate practicing physicians, patients, and industry concerning the rehabilitation of cardiac patients and to encourage cooperation between physicians in private practice and those in industry.

As part of a nationwide study of the rehabilitation of patients with cardiovascular disease, a detailed questionnaire was sent to the medical directors of a variety of industries in the United States to obtain information on the following questions: (1) general characteristics of the industries surveyed; (2) policies regarding employment of cardiacs; (3) actual number of known cardiacs hired; (4) magnitude of the problem, as reflected in the percentage of employees with heart disease, number of heart attacks, number of deaths due to cardiovascular disease, number of terminations due to heart disease, and absenteeism among employees during the preceding year; and (5) experience with workmen's compensation cases among cardiacs. We hoped, on the basis of information obtained in this survey, to better evaluate the problems involved in the rehabilitation of the cardiac in industry.

Although large in total number of employees, most of the industries surveyed were composed of autonomous plant units, often located in widely separated parts of the United States. This autonomy resulted in variations as to the amount of information concerning cardiac workers available because of differences in methods and types of health records, variations in availability of information contained in the records, and variations in the attention directed to the problems of the cardiac in the industry surveyed. Because of these problems and be-

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cause of the detailed nature of the questionnaire, it was possible for only 19 of the medical directors surveyed to provide us with sufficient information on which to draw conclusions for this study.

Results

Characteristics of the Industries Surveyed.—The types of industries surveyed are illustrated in table 1. They varied from life insurance and publishing

TABLE 1.—*Age Spread of Employees in Industries Surveyed*

Industry	Total Plant Population	Age, Yr., % Under 35	35-54	Over 55
Airplane manufacturing	31,655	32.8	55.6	11.6
Pharmaceutical	2,312	43.0	44.0	13.0
Petroleum products	7,156	25.2	58.6	16.2
Electric utility	26,106	19.8	55.5	24.7
Flour milling	1,900	44.0	46.0	10.0
Copper smelting	1,200	32.0	48.0	20.0
Chemical	1,900	25.0	50.0	25.0
Chemical	11,286	53.0	36.0	11.0
Communications	40,000	60.0	30.0	10.0
Battery manufacturing	999	...	51.0	49.0
Electrical appliances	30,000	55.0	35.0	10.0
Automobile manufacturing	10,870	41.0	40.0	19.0
Textiles	1,025	35.0	50.0	15.0
Publishing	4,664	25.2	44.4	30.4
Glass	8,000	37.0	53.0	10.0
Life insurance	17,347	60.0	36.0	4.0
Total	196,480	Av. 36.7	45.8	17.5
Chemicals	16,000			
Chemicals	11,000			
Glass	28,000			
Total	55,000 251,480			

to airplane manufacturing, flour milling, and copper smelting. The employees per industry ranged from approximately 1,000 to 40,000. A little over 30% of the workers surveyed were under 35 years of age, while 17.5% were over 55.

All 19 industries employed full-time physicians, and they all required preemployment physical examinations of their employees. Most of the examinations included chest roentgenograms for all employees and electrocardiograms for those over 40 or for those in whom the history or physical examination indicated the possibility of cardiovascular disease. In addition, periodic health surveys were done in the majority of industries, although usually only on executives. Only one of the industries had a mandatory periodic health survey of all employees.

The types of employees in the industries surveyed included executives, clerical or white collar workers, and skilled, semiskilled, and unskilled workers. The percentages of workers in each of these categories varied from industry to industry, but exact figures were not obtained and were not considered necessary for the purpose of this survey.

Policies Regarding Employment of Cardiacs.—Only 9 of the 19 industries had a stated policy to hire cardiacs. Seven industries had a definite policy against hiring such workers, while in three industries this information was not available.

In an attempt to determine what some of the factors might be that influenced the industries not to hire cardiacs, one of the questions asked was whether compensation, sickness benefit, or pension liability were of importance in determining employment policy. The answers were as follows: for compensation liability, 18 answered yes, and 1, no; sickness benefit liability, 17 answered yes and 2, no; and for pension liability, 16 answered yes and 3, no. It is apparent that concern regarding potential or possible liability in these three categories is of importance in the policies of certain industries regarding the hiring of cardiacs.

Number of Cardiacs Hired.—Eight industries reported that they had hired cardiacs during the past year. In this period 242 people with known cardiovascular disease were among the total of 19,321 new workers employed. Asymptomatic hypertension was the most common diagnosis, followed in order by rheumatic heart disease, heart disease type unspecified, and arteriosclerotic heart disease. Actually, only 24 of the new employees had been given a diagnosis of arteriosclerotic heart disease, despite the frequency of this disease in the adult male population of this country (table 2).

Magnitude of the Cardiac-in-Industry Problem.—Although the percentage of persons with diagnosed or existing cardiovascular disease varies greatly from industry to industry because of differences in the age of the employees and the percentage of males employed, it is likely, on the basis of information obtained in this survey, that approximately 8% of the employees in the industries surveyed had cardiovascular disease. This information was not available from all the medical directors, but, of those who reported, this was about the average figure.

TABLE 2.—*Types of Heart Disease Present in New Employees (Hired Within Past Year) in Eight Industries*

	Industries							Total
Total no. of employees hired	9,877	325	460	1,000	1,012	5,000	647	1,000	19,321
No. with cardiovascular disease hired	95	6	1	50	35	16	26	13	242
Arteriosclerotic heart disease	21	...	...	...	...	2	1	...	24
Rheumatic heart disease	5	3	...	20	...	10	5	10	53
Hypertension	55	2	...	30	...	2	13	3	105
Cerebral vascular disease	7	...	...	...	...	...	...	...	7
Peripheral arterial disease	2	1	...	...	...	2	...	...	5
Type unspecified	5	...	1	...	35	...	7	...	48

There was great variation in the number of employees reported to have suffered heart attacks in the past year. Two industries of approximately the same size reported that 120 and 4 employees, respectively, had suffered heart attacks. The 120 heart attacks reported by one industry, with 26,106 employees, constituted more than one-half of the total of the 226 reported by all the industries (table 3). Even if the figures reported by the one industry with the highest incidence of heart attacks were

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generally applicable to the industry it is apparent that this does not constitute a truly major problem for industry, but it is a factor which must be considered in view of changing practices in the administration and interpretation of workmen's compensation laws.

It must be realized, also, that the great majority of workers who suffer heart attacks return to work for their old employer, and a suitable job must be found for them if they are unable to perform their previous work. In our survey all 19 of the industries reported that it was their policy to return an employee to his job after recovery from an acute cardiac episode. Only one industry added any qualification, and that was "if a suitable job is available." This policy is of far more importance in the rehabilitation in industry of workers than are the policies regarding initial employment of cardiacs, because the vast majority of people who develop cardiovascular disease do so after they reach an age when they should be earning a living at work.

There were reported to be only 54 workers, exclusive of those who died, whose employment was terminated because of disability due to cardiovascular disease. Although there was considerable variation from one industry to another, this number appeared to be only a small percentage of the total number of workers whose employment was terminated (table 3).

The total number of deaths attributable to cardiovascular disease was 181 in an employee population of almost 170,000 (table 4). There were a few industries that did not have accurate information on this question, and their replies were, therefore, not included in the tabulation of these results. In considering the possible implications of these figures to workmen's compensation liability, it is of interest that only 13% of the deaths due to cardiovascular disease occurred at work, while 87% occurred off the job.

TABLE 3.—*Heart Attacks in Preceding Year in Eight Industries*

Total Plant Population	Heart Attacks During Past Year			No. of Workers Whose Employment Terminated Because of Cardiovascular Disease (Exclusive of Deaths)	% of Total No. of Workers Whose Employment Was Terminated
	Total	At Work	Away from Work		
26,106	120	12	108	30	18
1,960	3	1	2	1	33
11,200	16	8	8	4	20
1,900	4	2	2	...	...
40,000	37	0	37	10	24
30,000	4	2	2	3	— 1
1,025	18	3	15	3	±10
4,664	24	0	24	3	?
116,855	226	28	198	54	

Absenteeism is another factor which is often considered in the employment of any worker. Ten of the medical directors surveyed did not have specific information on absenteeism among employees known to have cardiovascular disease. Five indicated that absenteeism in this group was above the plant average, while four considered it comparable in the groups with and without cardiovascular disease.

Experience with Workmen's Compensation Cases Among Employees.—The possibility of workmen's compensation liability has become an increasingly important reason given by employers for their reluctance to hire workers known to have cardiovascular disease. That this may be more of a possible than an actual problem at the present time is indicated from the results of our survey. The entire group of industries, with three exceptions who did not have the information available, reported only 10 workmen's compensation settlements resulting from cardiovascular disease during the past five years. This is a relatively small number, considering the total number of employees and the probable number of acute episodes of illness due to cardiovascular disease which occurred at work during this period. The fact that there were so few compensation settlements may be due to the fact that there were good sickness or other benefits which helped the individual defray the cost of illness, and it also seems to indicate that on the whole the industries surveyed must have maintained good relations with their employees.

TABLE 4.—*Deaths Due to Cardiovascular Disease for Preceding Year in Ten Industries*

Total Plant Population	Deaths, Total No.	Deaths Occurring at	
		Home	Work
31,655	56	52	4
2,312	7	7	0
26,106	46	38	8
1,960	4 (2 not known)	1	1
1,200	7	0	7
1,900	3	1	2
40,000	47	47	0
30,000	7	5	2
28,000	1	1	0
4,664	3	3	0
167,797	181	155	24

Comment

The results of this survey confirm the previous report of Olshansky and others [1] that many employers are reluctant to hire cardiacs, even if they do not have a definite policy against it. They found in their greater Boston survey that only 99 known cardiacs were hired among 13,431 workers employed during a six-month period. In our survey we found that 242 persons with cardiovascular disease were hired among 19,321 new employees.

The factors which determine employment policy were found by Olshansky and co-workers [1] to include (1) workmen's compensation liability, (2) lack of suitable jobs, (3) sickness and health insurance liability, (4) low productivity, (5) absenteeism, and (6) limited in-plant mobility. In a survey of a variety of industries covering over 1,375,046

employees, Kline [2] found that the fact that physical demands of work exceeded the physical capacity of the cardiac was listed by 71% of the industrial physicians surveyed as a major reason for reluctance in hiring cardiacs. Next in order of importance were risk of monetary loss arising out of compensation claims, 42%; consideration of cardiacs to be a heavy burden on company-sponsored insurance programs, 30%; insufficient medical staff, 12%; and policy of the personnel department, 11%. Only 8% of the physicians surveyed considered cardiacs to be unsafe workers and only 3% considered them to be inefficient.

Our results agree with these earlier findings that the threat of monetary loss from compensation claims, sickness benefits, or pension benefits is a major reason cited by industries for their reluctance to hire cardiacs. The second major factor seems to be concern that the physical demands of available jobs are likely to exceed the capacity of the cardiac, particularly when the industries already have in their labor force a large number of employees (approximately 8%) with cardiovascular disease to occupy jobs which are considered to have physical stresses equal to the capacity of the cardiac. Other factors, such as absenteeism, low productivity, and safety, do not appear to be major factors in determining employment policy. As a matter of fact, it has been found by many physicians in industry, including Franco at the Consolidated Edison Company in New York,[3] Greer at the Gillette Safety Razor Company in Boston,[4] and Brown in the Railroad Industry in New South Wales, Australia,[5] as well as others,[6] that absenteeism among cardiacs is not a major problem. They are safe workers when properly placed; usually they have a higher average productivity than the noncardiacs, and the turnover among this group is below the average for noncardiacs.

The actual monetary loss to employers as a result of compensation settlements to cardiacs would not appear to be very high in comparison to the over-all cost of workmen's compensation. We found only 10 compensation settlements in a five-year period. Olshansky and co-workers [1] found that, of 100 employers, 22 had claims against them. There was a total of 78 compensation claims, but 45 of these were against a single employer. Although these numbers are not great, they still constitute a threat to any individual employer who hires cardiacs.

It is well for the practicing physician to be aware of some of the problems which physicians in industry and which industry in general consider important in the employment of cardiacs. It is particularly important for the practicing physician to realize that the great majority of industries will return an old employee to his job or to a job which is within his capacity if he suffers an acute cardiovascular illness during his tenure of employment. If the practicing physician appreciates the problems faced by the industrial physician he can aid his patient with cardiovascular disease to be productively placed in a job which is dangerous to neither himself nor his fellow employees, which he can perform with equal or greater skill than the noncardiac, and which, hopefully, does not impose added financial risk on the employer. In order to do this, however, the family physician must appreciate the fact that the great majority of cardiacs can work productively and safely if properly placed.

Many problems in the rehabilitation in industry of the worker with cardiovascular disease remain to be solved, but progress can be made by (1) education of physicians regarding the employability of most cardiacs; (2) education of the patient about heart disease and about his own capacity for work and enjoyment of life; (3) education of industry regarding the present state of our knowledge about work capacity of cardiacs and their absenteeism, productivity, and safety as well as the facts about compensation, sickness benefit, and pension liabilities; (4) continued research, both in industry and in the laboratory; (5) a broad legislative study of the whole field of workmen's compensation as recently recommended by Lane in his comprehensive review [7] in the hope that from this will come legislative changes that would either remove the degenerative diseases from the classification of industrial accidents or produce laws which would not be deterrents to the rehabilitation of the handicapped worker; and (6) continued and increased cooperation between the physicians in private practice and those in industry for the benefit of the patient.

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Summary

A questionnaire survey on the rehabilitation of workers with cardiovascular disease in industry has been carried out. The medical directors of 19 diversified industries operating plants in widely scattered areas of the United States and representing a total working force of approximately 251,000 participated. Only 9 of the 19 industries had a stated policy to hire cardiacs, and during the preceding year only 242 were hired in a total of 19,321 new workers employed.

Factors considered of importance in industry's reluctance to hire cardiacs included (1) possible compensation, sickness benefit, or pension liability; (2) the large number of cardiacs already employed who developed their disease while at work; (3) lack of suitable jobs for cardiacs in addition to those already employed, and (4) a variety of lesser factors.

The actual number of compensation settlements for cardiac cases was small in the industries surveyed so that at the present time this appears to be more of a possible than an actual threat of monetary loss to the employer.

Many problems in the rehabilitation of the cardiac worker in industry remain to be solved but progress can be made by (1) education of practicing physicians, patients, and industry; (2) continued research in industry and in the laboratory; (3) a broad legislative study of the whole field of workmen's compensation; and (4) continued and increasing cooperation between physicians in private practice and those in industry.

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CARDIAC REHABILITATION

QUESTIONNAIRE SURVEY OF GENERAL PRACTITIONERS

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As part of a nationwide study of the rehabilitation of patients with cardiovascular disease, questionnaires were sent to general practitioners and cardiologists asking their definitions of rehabilitation, especially as applied to persons with cardiovascular disease; their opinions about the major problems in rehabilitation of patients with cardiovascular disease; and their opinions as to how these problems might best be solved. They were also asked to comment on their own experiences in the rehabilitation of patients with cardiovascular disease. The opinions of the cardiologists will be reported elsewhere.[1] In addition, a group of industrial physicians were questioned as to their experiences relative to the rehabilitation in industry of persons with cardiovascular disease. These opinions are summarized in an accompanying report (see this issue, page 787).

This report is concerned with the opinions of 40 members of the Academy of General Practice from

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Rehabilitation, especially as applied to persons with cardiovascular disease is a positive action, the aim of which is to get the patient (and his relatives) in a healthy optimistic state of mind, and his body in as good functioning capacity as is possible, so that he may happily return to society as a producing, independent, creative member. The most important problem is the elimination of fear and misinformation about heart disease in the patient and his family. Using congenital heart disease as an example, the greatest situation to be overcome, in the rehabilitation of a patient, is the avoidance of problems resulting from over-restriction imposed by parent or doctor. Education of physicians, such as now practiced by the American Heart Association, to include such facilities that aid in the placement of cardiacs in suitable jobs, is one important approach to rehabilitation.

widely scattered areas of the United States. The questions asked and the answers given were as follows:

Question 1.—What would you consider a proper definition of rehabilitation, especially as applied to persons with cardiovascular disease?

Answer: A definition which included most of the ideas expressed by the group of general practitioners surveyed was that of Dr. Richard B. Elgosin of Hamden, Conn. Dr. Elgosin stated: "Rehabilitation is a positive action, the aim of which is to get the patient (and his relatives) in a healthy optimistic state of mind, and his body in as good functioning capacity as is possible, so that the patient may happily return to society as a producing, independent, creative member."

Question 2.—What do you believe are the major problems faced by the practicing physician in his efforts to rehabilitate individuals with cardiovascular disease?

Answer: The problems, as set forth by the general practitioners, are tabulated in the table. They are listed in order of their relative importance. The most important problem was considered to be the elimination of fear and misinformation about heart disease in the patient and his family. This was also considered to be the number one problem by the cardiologists surveyed.[1]

Major Problems Faced by Practicing Physician in His Efforts to Rehabilitate Patient with Cardiovascular Disease

	Degree of Importance		
	1	2	3
Elimination of fear and misinformation about heart disease	18	1	1
Economic problems faced by disabled cardiac patient	8	1	1
Finding of work within the patient's physical capacity	4	2	...
Lack of adequate time for family physician to counsel patient	3	1	...
Medical problems—including accurate diagnosis	3	...	...
Lack of trained personnel in related fields	1	2	1

The second most important problem was considered to be the personal economic problems faced by the cardiac. This reflects the awareness on the part of the family physician of the potentially devastating effect of heart disease on the patient's ability to earn a living. As the physician best acquainted with the patient and his family and the one who is aware of the environment in which the patient lives and works, the general practitioner is often in the best position to observe the economic problems. It is of interest that the cardiologists did not consider this to be a problem of major importance.[1]

Three physicians expressed particular concern about the lack of time in their busy practices to permit proper counseling of the cardiac patient. This is a problem which is faced by many busy practicing physicians, and it is one of the reasons why the patient must, at times, turn to the consultant cardiologist for such counsel and advice.

Question 3.—What do you think should be done to solve some of these problems?

Answer: There was general agreement by the general practitioners and the cardiologists regarding the principal solution to the problems of cardiac rehabilitation. Twenty-five of the 40 general practitioners queried thought that the most important single step in the solution to some of the present problems in cardiac rehabilitation could be made by education about heart disease. First, it was emphasized that education of the physician about heart disease could eliminate some of these problems, particularly iatrogenic heart disease and overrestriction of the cardiac. Education of the patient and his family about the more optimistic aspects of heart disease was considered to be a fundamental step in cardiac rehabilitation. It was thought that education of management and labor would result in more employment of cardiacs in industry. The view is shared by physicians in industry.

The educational efforts among physicians and the public by the American Heart Association and its affiliates was endorsed enthusiastically by the general practitioners, and it was frequently suggested that there should be further expansion in this field by the heart association.

Seven doctors felt the need of increased availability of facilities to aid in the placement of cardiacs in suitable jobs. Lack of such facilities in less populated areas of the United States was apparent from the responses to this question. Two doctors proposed increased availability of disaster insurance. Another wanted more rehabilitation centers, and yet another suggested adjustment of state compensation laws. The answers to this question contained a number of very valuable comments on cardiac rehabilitation, several of which follow:

1. Dr. Keith Hammond of Paoli, Ind., thought that there was first of all a need to emphasize that there is such a thing as rehabilitation in cardiovascular disease.

2. Dr. Stanley R. Truman of Oakland, Calif., thought that rehabilitation correlated more highly with attitudes and intelligence than with type of heart disease.

3. Dr. Harvey Runty of DeWitt, Neb., pointed out the hardy characteristics of the farm people who constitute his rural practice. Most of his cardiac patients wait too long to seek medical help, and after treatment it is difficult to enforce a proper degree of restriction. He practices "in a rural area where such a thing as malingering or being willing to 'set around' is practically unknown." He goes on to comment: "My patients have tremendous drive

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and ambition to keep working. It is not unusual to have patients work who have to stop and rest every 15 to 20 feet. They insist on milking, feeding cows, chickens, etc. They make treatments most difficult, but also after the acute phase, they rehabilitate quickly and without too much help."

Question 4.—In the order of their importance, what measures have you found of value in the rehabilitation of your cardiac patients?

Answer: Establishing a proper diagnosis, followed by indicated medical measures were considered to be basic steps in cardiac rehabilitation. After these immediate medical needs were met and the existing emergency subsided, the majority of physicians indicated that they proceeded with a discussion with the patient as to the nature of his illness and the likely degree of disability. This discussion was considered to be the most important of all the measures used in cardiac rehabilitation. To be effective, it was emphasized that this discussion should be completely unhurried.

Dr. James A. Blake of Hopkins, Minn., defined the nature of this discussion and the role of the family physician in cardiac rehabilitation as follows: "This discussion goes on continuously from the moment the diagnosis is made all through treatment, convalescence, and resumption of some type of work. It needs constant supervision of an interested, sympathetic, confident individual, and the general practitioner family physician is particularly needed here. For this reason he should be regarded as a full partner in all stages. This has been no particular problem to general practitioners in Minnesota, for we have full staff privileges in all hospitals, and there is a fine rapport between generalist and specialist." This comment not only defines the nature of this important discussion but eloquently emphasizes the place of the family doctor in cardiac rehabilitation.

Consultation with persons in related fields and use of ancillary agencies was reported by the general practitioners surveyed to have been of limited value. In many areas in which these doctors practice, such facilities are entirely lacking. Ministers were reported to have been the main source of extramedical help to the general practitioners and it was noted that when the patient had the advantage of faith, ministers were of particular value.

The fact that many physicians found such coprofessional services as vocational counseling and social service of limited value is illustrated by the comment of Dr. A. J. Franzi of San Francisco: "I regret to say that my experiences with social service and vocational counseling have been unhappy, in that too often I have lost the complete control over the patient's activity and felt that I was becoming an outsider in the care of my patient."

Question 5.—Please comment on your practical experience in the rehabilitation (including perhaps comments on ability to return to work, social and psychological adjustment) of patients with the following cardiovascular diseases:

(*a*) congenital heart disease, (*b*) rheumatic heart disease, (*c*) hypertensive cardiovascular disease, (*d*) coronary artery disease, (*e*) cerebral vascular disease, (*f*) neurocirculatory asthenia, (*g*) iatrogenic heart disease, and (*h*) luetic [syphilitic] heart disease and subacute bacterial endocarditis.

Answer: *a.* Experience with congenital heart disease by the family physician in this survey was limited by the relative infrequency of these disorders and by the specialized nature of both diagnosis and treatment in many of the patients with congenital heart disease. Most of these patients at one time or another are evaluated in the larger medical centers. It was acknowledged that the most dramatic illustrations of cardiac rehabilitation that could be recalled were those from this group that had been successfully rehabilitated after cardiac surgery. The avoidance of problems resulting from over-restriction imposed by parent or doctor on the patients whose lesions were functionally insignificant was considered to be an important principle to be followed in the rehabilitation of the patients with congenital heart disease.

b. In rheumatic heart disease results of cardiac rehabilitation were generally good when valve deformity was not great and when active rheumatic fever was not present. The patients belonging to this group were thought generally to make "a surprisingly good adjustment" and many carry on full activity with no restrictions. The value of surgery in selected cases was stressed, and the importance of meticulous medical management, particularly in the maintenance of an adequate penicillin prophylaxis, was also emphasized for patients in this group.

c. Considerably more pessimism about experience with patients with hypertensive cardiovascular disease was expressed by the general practitioners than by the cardiologists. Despite the use of antihypertensive drugs and the attention paid to the emotional needs of these patients, it was noted that they frequently did not feel well and were prone to discontinue treatment and often to drift from one physician to another.

d. Patients with coronary artery disease constitute the largest group. In general, favorable experience in returning the patients to work after an acute episode was reported. The role of the personal physician in educating the patient as to his potentialities following recovery from myocardial infarction was particularly emphasized. Experience was cited to show that most of these patients were able to return not only to work but to their previous occupation without a great deal of restriction.

e. Cerebral vascular disease, particularly when accompanied by hemiparesis or hemiplegia, constituted a particularly difficult problem in rehabilitation for the family physician. The need of specialized help including physical therapy, speech retraining, and vocational training was acknowledged, and it was apparent that these facilities were almost universally unavailable in rural areas.

f. For patients with neurocirculatory asthenia rather discouraging results were reported by the general practitioner. Emphasis was placed on the deep-seated psychiatric problems of these patients. One physician felt that he was successful in dealing with these patients if he was merely able to keep them out of bed.

g. Good results have been obtained in the group with iatrogenic heart disease when the intelligence and psychological status of the patients permitted insight into their problems. Several physicians noted that aid from cardiac consultants and continued cooperation between the cardiologist and family physician had solved a number of these problems.

h. Syphilitic heart disease and subacute bacterial endocarditis were universally described as being very infrequent in occurrence in the average general practice and afforded no particular opportunity for comment by the general practitioners surveyed.

Summary

Opinions about the rehabilitation of patients with cardiovascular disease have been obtained from members of the American Academy of General Practice who practice in widely scattered areas of the United States. It was apparent from the opinions of these family physicians that the most important steps in cardiac rehabilitation are those taken by the patient's personal physician—a position often occupied by a general practitioner of medicine. After meeting the medical needs of the patient, the most important step in returning the patient to an active and useful life was thought to be an unhurried explanation of the nature of the patient's illness, with emphasis on the more optimistic aspects of recovery whenever possible. In addition it was thought that this discussion should include advice from the physician regarding the ability of the patient to return to work and to a useful productive life. The elimination of fear about heart disease was thought to be the major problem faced by the general practitioner in his efforts to rehabilitate patients with cardiovascular disease. The solution to this problem was thought to lie in the education of the physician, the patient, and the family about the more optimistic aspects of heart disease.

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Malignant Lymphoma.—The treatment of malignant lymphoma varies with the nature and extent of the disease. Roentgen irradiation to localized glandular masses is still the best therapy. Survival time with x-ray treatment alone averages from four to six years, but by using intermittent treatment, patients have lived as long as 15 to 20 years. Dosages of 100 to 300 r's per treatment with a total of from 1000 to 3000 r over an extended period are used. Nitrogen mustard in doses of 0.2 mg. per kg. body weight is the best chemical treatment. This dose is repeated on the third day. Wintrobe's plan of treatment is as follows: chlorpromazine, 25 mg. at 4 hour intervals started 8 hours before administration of the nitrogen mustards is combined with 0.1 Gm. of Nembutal given at the time of mustard therapy (8 p. m.). If the patient is not asleep by midnight, the chlorpromazine and Nembutal are repeated, one dose each. Rarely is more than 0.6 mg. per kg. body weight used in a single course. Generally, the beneficial effects from a single course of nitrogen mustard therapy last longer than 6 weeks. In any event, serious toxic effects on the hemapoietic system can be prevented by avoiding administration of the agent or giving x-ray therapy oftener than at intervals of six weeks. TEM (Triethylene Melamine) at doses of 2.5 mg. per day on alternate days for four to six doses has led to excellent remission and has relieved troublesome itching. It is slower in action than the nitrogen mustards and is used only in those who cannot tolerate the mustard drugs. TEM is valuable . . . since it can be given orally. Because of cumulative effect, a selected dose of TEM is best given over a period of one to three days, with intervals of a month or longer between courses rather than more frequently as some have recommended. This should avoid serious toxic effects. Oral dosage is from 0.05 to 0.04 mg. per kg. body weight or about 5 to 25 mg. in a single course. Not more than 5 mg. should be given on any one day and better absorption is obtained if 2 Gm. of sodium bicarbonate are taken with each dose. TEM can be given intravenously at a dosage range of from 0.05 to 0.15 mg. per kg. body weight per course.—R. J. Brimi, M.D., Management of the Leukemias, *Journal of the Tennessee State Medical Association,* August, 1956.

HAZARDS OF THE IMMEDIATE POSTOPERATIVE PERIOD

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Since the introduction of postanesthetic observation or recovery rooms, the postoperative care of surgical patients has improved tremendously. There remains one further potentially dangerous, oft-neglected period, that between the end of an operation and the transfer of care to recovery room personnel. As an operation draws to a close, there is a natural tendency for all concerned to "let down." The pressures associated with the surgical procedure are over, and with the understandable desire to relax attention may be diverted from the patient. The surgeons usually leave the room. Often the anesthetist is left alone. Yet, at this time a number of events may transpire which will pose a threat to the patient's welfare. Removal of an endotracheal tube can be followed by many hazards. If a high oxygen concentration has been used during anesthesia, its replacement with room air can have untoward consequences. Vomiting may occur. Emergence excitement may develop. Pain may begin to be experienced by the patient, and fear and anxiety become manifest. Hypotension may be associated with change of the patient's position as he is moved from operating table to bed or litter. Atelectasis, emboli, pneumothorax, or the sequelae of inadequate treatment of blood loss may escape detection. The consequence of these and other problems will be discussed.

The surgical patient's welfare may be threatened by situations that develop in the interval between the termination of the operation and his arrival in the recovery room. It is essential that his condition be watched closely while his position is changed, the level of anesthesia is reduced, and the endotracheal tube is removed. This is particularly true if transfusions have been given for blood loss, respiration has been depressed by relaxants, or other factors exist that favor hemorrhage, embolism, anoxia, or vomiting. The excitement stage sometimes seen during induction has its counterpart in a delirium that sometimes occurs during emergence; the latter can be a traumatic experience to all concerned unless it is properly dealt with. The three primary causes for alarm are hypotension, respiratory obstruction or depression, and excitement. They must be watched for before and during the transportation of the patient to the recovery room.

Arterial Hypotension

When the anesthetist is busy disconnecting the anesthetic machine, turning off cylinders, and making preparations to move the patient from the operating room, he may not observe blood pressure or pulse for a 5-to-15-minute interval. A decrease in blood pressure is not uncommon at this time and may have reached serious proportions before it is recognized. The following factors have been identified as contributing to this inadequacy of circulation; others probably exist.

1. *Change of Patient's Position or Movement.*—It is known that passive tilt to head-up position can be followed by hypotension even in normal subjects. If compensatory reflexes are impaired by the administration of narcotics (fig. 1), ganglionic blocking drugs, or local vasodilator substances, postural hypotension may be marked.[1] The mechanism appears to be a pooling of blood in the dependent lower extremities, with a reduction in circulating blood volume. This alteration is probably the basis for the hypotension that develops when the patient's legs are returned from the lithotomy to the supine position at the end of the operation (fig. 2). Awareness of this possibility is essential. Prophylaxis consists in binding the legs from toes to groin with tight bandages prior to change in position. The precaution is also indicated at the end of prolonged operations, after those accompanied by major degrees of blood loss, and in debilitated patients. Despite this precaution, blood pressure should be recorded as soon as the legs are lowered. If hypotension occurs, the legs should be elevated again. Change in position from the lateral to the supine may also be followed by hypotension.

Movement of the anesthetized patient can cause a reduction in blood pressure. This may follow transfer from operating table to litter or bed, wheeling the litter from the operating room, or, if the patient is taken directly to his room, the jarring motion of an elevator. We have seen cardiac arrest as a patient was lifted from the operating table and transferred to the litter. Similar catastrophes have occurred during transport of anesthetized patients in elevators. The physiological basis for this hypotension has not been determined, but pooling of blood in the periphery, perhaps in the deep back muscles, is probable. Stimulation of cutaneous or

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proprioceptive receptors by jouncing may be involved, since hypotension has been observed as air currents were blown over the skin of anesthetized patients, or a painless skin incision made in a patient anesthetized by subarachnoid block. Local axon reflexes leading to redistribution of blood may

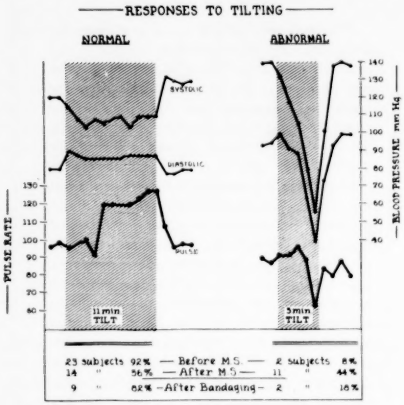

Fig. 1.—Effect of intramuscular administration of morphine sulfate in doses of 16 to 20 mg. on circulatory response to 70-degree head-up tilt in 25 subjects.

be the factor here. The hypotension associated with change of position and movement demands further study.

2. *Reduction in Level of General Anesthesia.*—As an inhalational drug is eliminated, nonvolatile depressants metabolized, or muscle relaxants detoxified, changes in a patient's circulation take place. "Cyclopropane shock" is a case in point.[2] At the end of an operation with this substance as the anesthetic, hypotension may develop. Reduction of a previously elevated arterial carbon dioxide tension has been implicated. The thesis is that inadequate pulmonary ventilation during anesthesia occurs more frequently than is appreciated. As a result, carbon dioxide accumulates and tends to elevate blood pressure through centrally mediated vasoconstriction. As anesthesia terminates and alveolar ventilation improves, arterial carbon dioxide tension is lowered. With a lessened central stimulation, vasomotor activity decreases and blood pressure falls. A similar sequence of events can follow the administration of any anesthetic, such as the combination of thiopental sodium and a muscle relaxant, which also may cause respiratory depression and respiratory acidosis.

Other changes follow completion of an operation with the patient under general anesthesia. When a closed-system method of administration has been used, removal of the anesthetic is accompanied by reduction in respiratory resistance, reduction in the temperature and humidity of the inspired air, and reduction in the oxygen concentration. Any or all of these could be implicated in the development of hypotension.

3. *Unrecognized or Inadequately Treated Blood Loss.*—Failure to measure and replace obvious blood loss during extensive operations may contribute to immediate postoperative hypotension in a patient. Blood loss may be hidden temporarily after closure of the thoracic or abdominal cavities, even though drains are in place. Obstruction to outflow through these drains can occur, and bleeding is not apparent.

There are certain clinical situations in which prolonged and profound oozing of blood may occur. The lungs, pancreas, prostate, and uterus appear to liberate substances which interfere with coagulation. Operations on these organs may therefore be accompanied by generalized oozing from the operative site. Transfusions of large volumes of banked whole blood may also be followed by oozing, which is difficult to control. The mechanism of this is still uncertain, but it may include the effects of excess amounts of citrate and heparin-like substances, reduced levels of accelerator globulin, platelets, and fibrinogen, and fibrinolysis. When massive transfusion is required, the anesthetist must be alert to the possibility of continued, generalized oozing. Use of fresh frozen plasma or fresh (one to three hours) whole blood has proved helpful in improving clot formation, as has the intravenous injection of 10% calcium gluconate.

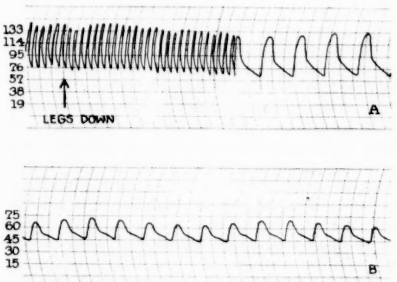

Fig. 2.—Continuous intra-arterial pressure pulse tracings in a 71-year-old patient after operation performed in lithotomy position. Time between charts A and B is two minutes. Pressures are in millimeters of mercury.

4. *Emboli.*—Hypotension following embolization has been mentioned. Although uncommon, pulmonary embolism may be the cause of sudden hypotension at the end of an operation. We have been bewildered by several such cases until postmortem findings revealed the cause. Cerebral emboli follow-

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ing mitral commissurotomy commonly cause intractable arterial hypotension. Other emboli may consist of fat or air.

Respiratory Sequelae

Hypoxia is a constant threat in the immediate postoperative period. Studies of Comroe and Botelho have indicated the unreliability of cyanosis in the clinical recognition of arterial anoxemia.[3] One must guard against the possibility of unrecognized hypoxia, since the signs and symptoms may be elusive. A patient should not be moved from the operating room until the anesthetist is certain about the adequacy of pulmonary ventilation and oxygenation. The following factors are the primary causes for alarm in inadequacy of respiration.

1. *Soft-Tissue Respiratory Obstruction.*—Partial or complete respiratory obstruction is a common phenomenon in the immediate postoperative period. In addition to the observance of thoracic movement, the anesthetist should place the palm of his hand over the patient's mouth and nose so as to appreciate the exhalation of air with each breath. The adage that noisy breathing is obstructed breathing is valid, and stertor calls attention to the abnormality. With complete obstruction, however, one must rely on the detection of respiratory muscle activity and the absence of movement of air against the sensing hand. Patients must be transported in a manner designed to forestall airway obstruction. The lateral position is safer than the supine in this regard. We have observed death from undetected respiratory obstruction during transportation of anesthetized patients.

2. *Vomiting.*—Vomiting at the conclusion of an operation while the patient is still on the operating table is welcomed by many anesthetists, since it may eliminate material which, if retained, might cause continued nausea and retching. So long as gastric contents are not aspirated into the respiratory tract, no harm is done. A high index of suspicion by the anesthetist affords the greatest protection for the patient. Anyone who has been anesthetized may vomit. Although swallowing often precedes vomiting, occasionally fluid may well up into the pharynx without prior warning. All these factors must be remembered as the operation comes to an end.

The 10-to-15-degree head-down tilt recommended by many has little value, for, if the mouth or pharynx contains vomitus at the time of an inspiration, inhalation of the material is likely. Nor is excessive stimulation of the pharynx with a suction catheter recommended. This can often be the cause of further gagging and vomiting. A properly functioning suction apparatus must be at hand, but it should be used judiciously. Similarly, an oral airway should not be permitted to remain in place too long, for its presence can stimulate vomiting as anesthesia lightens. When vomiting is anticipated, the head should be turned to the side.

If gastric contents enter the respiratory tract, we believe that repeated irrigation with 10 to 20 ml. of sterile saline solution introduced through an endotracheal tube is of value. This dilutes irritant acids or alkalies. The lungs can quickly absorb large quantities of saline solution. Unless particulate matter is aspirated, we do not believe that bronchoscopic aspiration is superior to the technique just described.

3. *Removal of Endotracheal Tube.*—If an endotracheal tube is withdrawn during a light plane of anesthesia, this stimulus may result in closure of the glottis. Laryngospasm can be marked and troublesome, particularly in infants and children. With their high metabolic rate and small residual volume of oxygen, hypoxia can develop quickly in these patients. This complication can be minimized by gentleness during extubation, extubation during deeper planes of anesthesia, or extubation after the patient awakens. Once laryngospasm has developed, frantic efforts to inflate the lungs with oxygen may cause instead inflation of the stomach, elevation of the diaphragm, and the likelihood of vomiting. Steady but not excessive pressure to a breathing bag containing oxygen is preferable and is usually sufficient. The intravenous injection of succinylcholine chloride to relax the striated muscle of the larynx, followed by manual pulmonary ventilation, may be needed. Should neither method be available, insertion of a large-bore needle (14 gauge) into the trachea below the cricoid cartilage may be lifesaving. Through this needle one can inject air with a large syringe or give oxygen via a rubber tube.

Removal of an endotracheal tube may also reveal for the first time that vocal cord paralysis has occurred during operation. After operation on the thyroid gland signs of respiratory difficulty may indicate such damage. Inspection of the vocal cords will reveal absence of movement with respiration. The surgical team should be alerted to the possible need for tracheostomy.

4. *Diffusion Anoxia.*—At the end of an operation with the patient under nitrous oxide anesthesia, the pulmonary alveoli and blood contain nitrous oxide and relatively small amounts of nitrogen. With the first inhalation of room air, nitrogen begins to diffuse into the blood and nitrous oxide into the alveoli. Because of its greater solubility in blood, the volume of nitrous oxide available for diffusion outward into the lung is considerably greater than the volume of nitrogen that replaces it in blood. Hence, there is a net gain in the gas volume of the lung. With the trachea patent, the lung does not expand but merely expels the mixture of gases and with it some oxygen. The residual oxygen is diluted and the partial pressure decreased by the outward dif-

fusion of nitrous oxide.[4] Even a few breaths of room air during inhalation of 80% nitrous oxide, as for replacement of a mask or aspiration of the endotracheal tube, can result in a decreased arterial blood oxygen saturation. Prevention of this complication consists in provision of a high oxygen concentration as nitrous oxide is being eliminated.

5. *Pneumothorax.*—We have observed pneumothorax following brachial plexus or intercostal nerve block, after rupture of an emphysematous bleb, in association with mediastinal emphysema, during dissections in the neck, when air had not been adequately withdrawn after thoracotomy, or during operations beneath the diaphragm. Examination of the chest must be carried out to identify this abnormality, for, should a tension pneumothorax be present, prompt aspiration of the air is essential.

6. *Pulmonary Atelectasis.*—Collapse of parts of the lungs behind bronchial obstruction must also be considered. This can occur with the patient under general anesthesia and remain undiagnosed, because the inhalation of a high concentration of oxygen prevents the recognition of hypoxia. When room air is breathed at the conclusion of the operation, the effects of atelectasis are unmasked. Again, physical diagnosis looms large in the recognition of this entity.

7. *Respiratory Depression from Muscle Relaxants.*—At the completion of an operation with the patient under an anesthesia which involves use of one of the muscle relaxants, respiratory inadequacy may prevail. These drugs reduce respiratory minute volume as a result of the neuromuscular blocking action upon intercostal muscles and diaphragm. Effects upon central regulatory respiration mechanisms may also prevail. If these pharmacological actions have not disappeared completely by the end of the operation, pulmonary ventilation must be assisted, lest hypoxia supervene. This undesirable sequela has occurred with all the muscle relaxants, even the short-acting members of the group.

8. *Restrictive or Obstructive Dressings.*—Insufficient alveolar ventilation may be caused by the application of excessively tight surgical dressings after such operations as radical mastectomy. Respiratory obstruction may also be caused by dressings or plaster casts applied about the head and neck. Surgeons must be warned of this possibility as the wound is being covered.

Immediate Postoperative Pain and Restlessness

As surgical patients emerge from general anesthesia, many are restless and complain of pain or discomfort. Restlessness may be of such severity as to deserve the term "delirium." Under these latter conditions restraints are essential, control of the wildly excited patient is difficult, and therapy may be urgently needed. The cause of this restlessness is uncertain. Incisional pain is a factor. Muscle strain and fatigue caused by awkward positions appear to be contributory. Repressed fears and anxiety play a role. A distended urinary bladder has been implicated. The pharmacological basis for the restlessness and agitation may be the same as that responsible for the excitement, struggling, and occasional delirium seen during the induction of inhalation anesthesia. The two phases might be likened to mirror images, the one occurring at the beginning and the other at the end of general anesthesia. Release of cortical inhibitions and loss of control over one's emotions and behavior are evident in both instances.

Regardless of the etiological background, one therapeutic approach is the administration of narcotic analgesics, either by vein or intramuscularly. Smaller doses of the drug are required under these circumstances than if the patient has fully awakened and is complaining primarily of pain. If restlessness is manifest before consciousness has returned, the analgesics often return the subject toward the anesthetized state. An intravenous injection is particularly likely to have this effect. This was described by Claude Bernard a century ago.[5]

Prevention of postoperative excitement is not always possible, but some measures appear to offer some success. Those patients who are excessively disturbed emotionally prior to operation or who have evident psychological difficulties should receive additional preanesthetic sedation. The administration of scopolamine is best omitted in the case of these individuals, for its use, particularly in combination with a barbiturate, has been associated with an increased incidence of emergence excitement in our clinic. A small dose of a narcotic analgesic, injected intramuscularly prior to the conclusion of anesthetization, seems to result in smoother awakening. The patient's circulatory balance should be judged adequate before such a drug is given.

Treatment of the agitated individual includes a number of possibilities. If the patient has been in one position upon the operating table for a long period of time, this position should be changed in the bed or the litter. If pain is a factor, a small dose of narcotic (morphine, 5 mg., meperidine [Demerol] hydrochloride, 15 to 25 mg., or anileridine [Leritine], 10 mg., administered intravenously or intramuscularly) is indicated. Chlorpromazine (Thorazine) hydrochloride, in doses of 2.5 to 5.0 mg., or apomorphine hydrochloride, 1.0 to 1.5 mg. in 5 ml. of saline solution, given slowly by vein is often effective. A final method of controlling postoperative excitement is the intravenous administration of a cerebral cortical stimulant, such as caffeine and sodium benzoate or nikethamide.

These medications are not without hazard. All may cause hypotension, retching, and vomiting. The hypotension after the injection of chlorpromazine and less frequently after the administration of a narcotic may be profound. Fortunately, as the anesthetics are eliminated and self-control is reestablished, agitation lessens, and the patient be-

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comes quiet. Time therefore is on one's side. The experience, however, may be a traumatic one, not only for the patient but for his attendants as well.

Summary

The period between the end of an operation and admission to a recovery room poses distinct hazards to the surgical patient. Hypotension, inadequacy of respiration, and disturbing excitation are the primary causes for alarm. The etiological and therapeutic aspects of these three conditions have been considered.

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PARAVERTEBRAL ALCOHOL BLOCK OF LUMBAR SYMPATHETIC NERVES

EVALUATION BY SWEATING TESTS IN THREE HUNDRED FIFTY-ONE PATIENTS

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Paravertebral injection of alcohol for the purpose of blocking lumbar sympathetic ganglions was carried out in 351 patients with peripheral occlusive vascular disease (97% of cases), popliteal aneurysms, causalgia, or hyperhidrosis. The total number of injections was 454, since some were bilateral and others were repeated. Premedication and local anesthesia were used to facilitate injection, and 4 cc. of absolute ethyl alcohol was given in each case. The extent of the resulting sympathetic blocking was determined by a sweating test. This consisted of painting an alcoholic solution of cobaltous chloride on the dry skin and noting the change from deep blue to bright pink in those areas where sweating could still be induced. Adequate sympathetic blocking was achieved in 65% of all treated patients. Side-effects included neuralgia, which occurred in 10 patients and which was controlled by physical therapy. The value of alcohol block in cases of intermittent claudication was not demonstrated, but other evidence of improved circulation was obtained. This procedure is a substitute for lumbar sympathectomy and has given symptomatic relief in cases where operation was refused or contraindications for operation existed.

The first injection of alcohol into the trigeminal nerves was carried out by Schlösser [1] in 1903 as an effective treatment of trigeminal neuralgia. In the following years Ostwalt,[2] in Paris, reported some modifications of this treatment. However, he gave full credit to Schlösser for the original technique, which had been demonstrated to him during a visit to Schlösser's clinic in 1904. Lévy and Bandouin in 1906 published their modification of the techniques of Schlösser and Ostwalt.

In 1923 Läwen,[3] in Germany, inspired by Bergmann, Kappis, Danielopolu, and Hristide, injected procaine hydrochloride (Novocain) paravertebrally into the sympathetic nervous system for anesthetic, diagnostic, and therapeutic purposes in abdominal disorders and in cardiac pain. At first Läwen and his collaborators had little success in the treatment of patients with angina pectoris, but in 1924 Brunn and Mandl [4] reported the successful treatment of several patients by means of the paravertebral injection of procaine into the sympathetic nerves. To prolong the effect, Brunn suggested the use of alcohol as a blocking agent. In this country Swetlow reported at a meeting of the New York Neurological Society in 1925 the

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† Dr. Osborn died July 30, 1957.

first case of congenital syphilitic heart disease in which precordial pain was treated effectively with a paravertebral injection of alcohol. In 1926 Swetlow [5] reported several cases in which angina pectoris was treated satisfactorily with a paravertebral alcohol block of the thoracic sympathetic nerves.

During the next few years the Whites [6] and others used both procaine hydrochloride and alcohol in the treatment of angina pectoris. The first paravertebral injection of alcohol into the lumbar sympathetic nerves was reported in 1930 by Stern [7] in three cases of thromboangiitis obliterans (Buerger's disease); he observed definite increase of the circulation in the extremity after the block. In 1931 Flothow [8] preceded the alcohol block by a diagnostic injection of procaine and reported excellent results in 50 patients with various

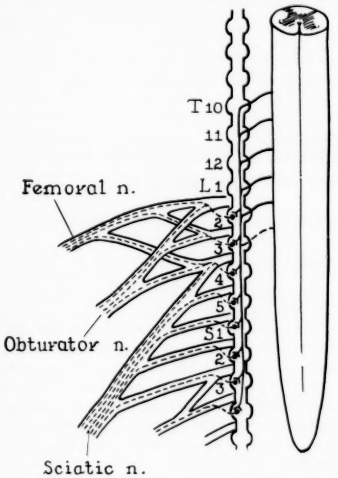

Fig. 1.—Sympathetic innervation of lower extremity. Preganglionic fibers originate from 10th thoracic segment to 2nd or 3rd lumbar segment of spinal cord. Postganglionic fibers arise segmentally in paravertebral ganglions and are distributed segmentally to nerve roots of femoral, obturator, and sciatic nerves.

peripheral vascular deficiencies. Reichert gave paravertebral injections of alcohol into the lumbar sympathetic nerves to relieve intermittent claudication and observed "striking results" in 25 patients.

In 1926 Brown [9] reported an absence of sweating from the knees down after bilateral removal of the second, third, and fourth lumbar sympathetic ganglions and the included sympathetic trunk. Since that time, absence of sweating has been used to measure the completeness of sympathetic denervation. A simple method for determining the lack of sweating was introduced by one of us [10] in 1935.

During the intervening years various reports have been made on technique, complications, success, and duration of paravertebral alcohol blocks on a limited number of patients. Because many sweating tests have been carried out on those of our patients receiving alcohol injections, the present study of 351 cases was made to determine the completeness and the duration of the denervation and to determine the frequency of complications associated with these blocks.

Anatomy

The sympathetic nerves to the lower extremities arise as follows (fig. 1). The preganglionic nerve cells are in the lateral gray masses in the spinal cord, from approximately the 10th thoracic segment to the 2nd or 3rd lumbar segment. The preganglionic fibers leave the spinal cord segmentally by way of the anterior root and are then carried by white rami to the paravertebral ganglions. A synapse occurs in the paravertebral ganglions at the level of the emergence of the preganglionic fibers from the vertebral canal in the paravertebral lumbar chain of ganglions or above or below it.

The postganglionic cell bodies lie in the paravertebral ganglions, and fibers leave the ganglions via the gray ramus to join the somatic nerves. The somatic and sympathetic nerves supply the lower extremities by the obturator, femoral, and sciatic nerves. The paravertebral ganglions in the lumbar and sacral regions are somewhat variable in number but, in general, lie close to the somatic nerves which they supply with postganglionic sympathetic fibers.

Inasmuch as there is no sympathetic outflow from the spinal cord below the second or the third lumbar vertebra, the sympathetic components of the sciatic nerve are readily interrupted by blocking the second and third lumbar ganglions. The obturator and femoral nerves, however, are also supplied by the first lumbar somatic nerve root and the adjacent sympathetic ganglion. It is necessary, therefore, to interrupt the first lumbar sympathetic ganglion, along with the second and third ganglions, to produce adequate sympathetic denervation of the entire leg.

Technique of Paravertebral Alcohol Block

The therapeutic blocks in our cases were not the endeavor of only one person but were the combined effort of all members of the Section of Anesthesiology. Before paravertebral block was scheduled, the patient was seen in consultation by a member of the Section of Neurologic Surgery to determine whether surgical or chemical interruption should be performed.

The technique used by the various anesthesiologists for insertion of the needle has been based on the technique of Lundy. In the last few years the one-needle technique has been used in most cases. This single needle is placed at the level of the second lumbar vertebra. From the results obtained, the placement

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of the needle at this level has been as effective as the placement of the needles at the level of the second and third and even the fourth lumbar vertebrae.

The patient is told to take neither food nor drink after 6 p. m. on the day before administration of the block. Preoperative medication, if given, consists of a short-acting barbiturate, atropine and morphine, or

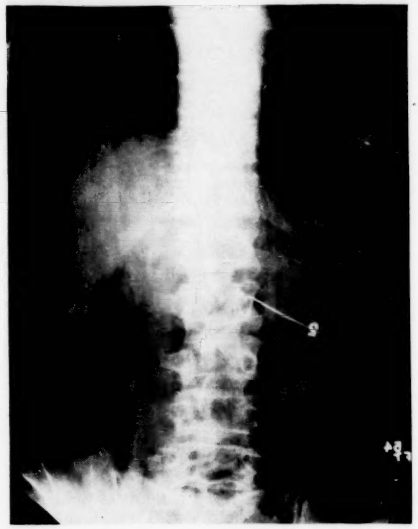

Fig. 2.—Anteroposterior roentgenogram, showing placement of needle at level of second lumbar vertebra. Level of needle at entrance into skin approximately opposite spine of second lumbar vertebra. Note angulation of needle cephalad, so that its tip lies in about midway between top and bottom of vertebra. Lead no. 2 identifies at what level anesthesiologist believed needle was placed. If needle was ill-placed, another needle with different lead marker would be utilized, to properly differentiate two films.

meperidine (Demerol) hydrochloride. Prior to the patient's arrival in the operating room, a table or cart is prepared with an x-ray cassette holder in place, so that roentgenograms can be readily taken without moving the patient once the needle or needles are in place. The procedure is carefully explained to the patient, and the possibility of complete or partial failure of the block and the remote, but definite, possibility of alcohol neuritis are pointed out.

With the patient in a prone position on the cart, the spine of the second lumbar vertebra is palpated. At this level and approximately 4 to 5 cm. from the midline a wheal is made with a local anesthetic agent, and the local anesthetic agent is then injected down to the level of the transverse process. A 120-mm. needle is inserted and slightly angulated cephalad, so that it is advanced along the lateral border of the second lumbar vertebra until it comes to rest at, or slightly below (anterior to), the anterolateral border. Anteroposterior and lateral roentgenograms are then taken to determine the exact position of the needle (fig. 2 and 3).[11] If the needle is well placed, no further roentgenograms are needed. If the needle is ill-placed, it is manipulated or another needle is inserted, and another roentgenogram is made.

The patient is then given intravenously a small amount of thiopental (Pentothal) sodium for analgesia, and 4 cc. of absolute alcohol is injected through the lumbar needle, with frequent aspiration via the needle to make sure that there is no intravascular injection. If a bilateral block is to be done, then 4 cc. of alcohol is injected on each side. The patient is allowed to awaken and is returned to his room. Within 24 to 48 hours after the block, a sweating test is carried out to determine the efficacy of the block.

Fig. 3.—Lateral roentgenogram, showing that position of needle in depth relationship is correct. When it is correctly placed, point of needle is just ventral to anterolateral surface of vertebra. Sweating pattern for patient was excellent.

Sweating Test

The sweat glands are innervated by the thoracolumbar or sympathetic division of the autonomic nervous system. Sweating induced by heating the body occurs

as a reflex mediated through the central nervous system and the sympathetic nerve fibers to the sweat glands.[12] Segmental regions of anhidrosis in man after sympathectomy or chemical destruction of the sympathetic rami and ganglions indicate the completeness of the sympathetic interruption.

The method used to determine the presence or the absence of sweating is a colorimetric one based on the chemical fact that, when cobaltous chloride in a saturated alcohol solution is painted in stripes on the dry skin, it has a deep blue color but turns to bright pink on the addition of water or sweat. The solution on the skin dries readily if it is put on in small quantity. To produce sweating, an aluminum heat cabinet,

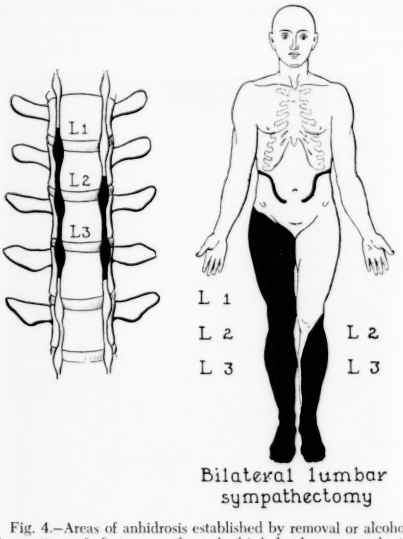

Fig. 4.—Areas of anhidrosis established by removal or alcohol destruction of first, second, and third lumbar sympathetic ganglions or second and third lumbar sympathetic ganglions.

containing a series of incandescent bulbs and large enough to cover the entire body except the head, is placed over the patient. A temperature of 130 F is maintained until sweating is induced, usually for 10 to 12 minutes. If sweating is delayed, a hot drink will hasten its appearance. The heat cabinet then is removed, and the portions of skin to which the solution has been applied are observed immediately. Where sweating has occurred, the dots or stripes of solution are bright pink. In places where varying degrees of sweating can be observed, the transition may be noted with considerable accuracy by observing the change in color of the stripes. On humid days sufficient moisture may be present in the air to change the color in the solution, but it is never the deep pink observed in the presence of sweating. Furthermore, the heat cabinet eliminates the factor of atmospheric moisture.

Results as Indicated by Sweating Test

The results of the paravertebral injection of alcohol into the lumbar sympathetic nerves, which we are reporting in our 351 cases, were based on the anhidrosis

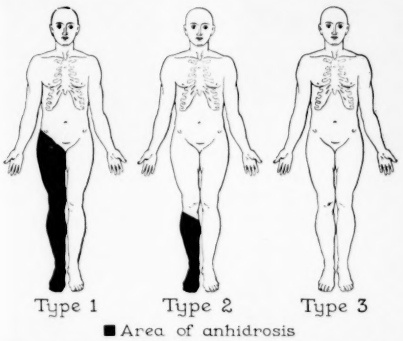

Fig. 5.—Three types of sweating pattern after paravertebral injection of alcohol into lumbar sympathetic nerves. Type 1 corresponds to blocking of first, second, and third lumbar sympathetic ganglions. Type 2 corresponds to blocking of second and third lumbar sympathetic ganglions. In type 3 no blocking effect was obtained.

found after operation. Three patterns of anhidrosis and, therefore, three types of results were found: (1) anhidrosis such as is caused by complete block of the first, second, and third lumbar sympathetic ganglions; (2) anhidrosis such as is caused by complete block of the second and third lumbar sympathetic ganglions; and (3) completely unsatisfactory results characterized by spotty anhidrosis or absence of anhidrosis in regions corresponding to the first, second, and third lumbar segments (fig. 4 and 5).

Results are listed in tables 1 to 5, the patients being divided into various groups. In table 1 results are given for 280 patients who had unilateral alcohol blocks

TABLE 1.—*Unilateral Paravertebral Alcohol Blocks of Lumbar Sympathetic Ganglions*

Anhidrosis Indicating Ganglions Blocked	Patients No.	Patients %	Total Blocks	Repeated Blocks
Type 1 (L-1, L-2, L-3)	103	37.8	110	7 on 7 patients
Type 2 (L-2, L-3)	65	23.2	68	3 on 2 patients
Type 3 (unsatisfactory)	112	40.0	136	24 on 20 patients
Total	280	100.0	314	34 on 29 patients

and in tables 2 and 3 for the patients with bilateral blocks. In 32 of the patients who had bilateral blocks, a symmetrical pattern of anhidrosis was obtained (table 2) in the two extremities, and in 22 patients, it was not symmetrical (table 3). Results on 17 pa-

tients who had long-lasting sympathetic denervation (up to five years) as proved by the sweating tests are given in table 4. The results of all paravertebral alcohol blocks of the lumbar sympathetic ganglions, performed during the past five years at the Mayo Clinic, are given in table 5.

TABLE 2.—*Bilateral Paravertebral Alcohol Blocks of Lumbar Sympathetic Ganglions*

Anhidrosis Indicating Ganglions Blocked	Patients No.	Patients %	Total Blocks	Repeated Blocks
Type 1 (L-1, L-2, L-3)	13	40.6	29	3 on 2 Patients
Type 2 (L-2, L-3)	7	21.9	16	2 on 2 patients
Type 3 (unsatisfactory)	12	37.5	24	None
Total	32	100.0	69	5 on 4 patients

Sixty-five per cent of the patients obtained either complete anhidrosis of the lower extremity (type 1) or clinically satisfactory anhidrosis (type 2), especially in thromboangiitis obliterans which affects mostly the smaller peripheral arteries. The remaining 35% had unsatisfactory results from blocks.

Comment on Results

The lumbar sympathetic ganglions vary in number and location. Ray and Console [13] pointed out that return of sympathetic activity after sympathectomy for peripheral vascular disease and hypertension is not usually due to regeneration of the sympathetic nerves; rather it is due to additional sympathetic pathways which do not pass through any part of the sympathetic chain. Roth and Craig [14] confirmed this by means of the sweating test. In their series lumbar sympathectomy was performed 283 times on 183 patients with

TABLE 3.—*Bilateral Miscellaneous Paravertebral Alcohol Blocks of Lumbar Sympathetic Ganglions*

Anhidrosis Indicating Ganglions Blocked	Patients No.	Patients %	Total Blocks	Repeated Blocks
Type 1, unilateral Type 2, unilateral	19	86.4	37	None
Type 2, unilateral Type 3, unilateral	3	13.6	9	3 on 2 patients
Total	22	100.0	46	3 on 2 patients

peripheral vascular disease. The expected complete denervation from the toes to the inguinal region occurred after only 7.4% of the lumbar sympathectomies. In 21.6% of the patients the region of anhidrosis extended from the midthigh to the toes, in 40.6% from the knee to the toes, and in 30.4% from below the knee to the toes.

Hollinshead [15] anastomosed the cephalic end of the cervical sympathetic trunk, after removal of the superior ganglion, with the distal end of the median or the ulnar nerve of the cat. He demonstrated that the regenerating sympathetic fibers failed to reach the sweat glands, the return of sweating being due to an ingrowth of fibers from the intact radial nerve, and suggested that there is a limitation in the length to which preganglionic fibers can grow. No evidence was obtained that preganglionic fibers might replace postganglionic fibers to produce anomalous sweating in man after removal of the sympathetic chain.

Alexander and associates [16] and Lowenberg and Morton demonstrated by dissection of cadavers the absence of the first lumbar ganglion. Ganglion cell aggregates were found as extraganglions either adjacent to the ventral nerve roots or embedded in the ventral spinal nerve roots at the site of origin of a white communicating ramus and in its proximal portion in the first and second lumbar segments only. The most frequently found ganglion at its expected level is the second lumbar ganglion. Gruss,[17] as early as 1932, observed ganglions in the white and gray communicating rami in man. It can be believed that these ganglion cells are synaptically connected with preganglionic fibers, thus forming conduction pathways. Sweating patterns of types 2 and 3 were believed to result from these conductive sympathetic pathways, anatomic variations in location of the ganglions, or changes in the technique.

TABLE 4.—*Long-Lasting Paravertebral Alcohol Blocks of Lumbar Sympathetic Ganglions*

Anhidrosis Indicating Ganglions Blocked	Patients No.	Patients %	Total Blocks	Repeated Blocks
Type 1 (L-1, L-2, L-3)	10	58.8	13	3 on 3 patients
Type 2 (L-2, L-3)	7	41.2	12	5 on 3 patients
Total	17	100.0	25	8 on 6 patients

Indications for Paravertebral Lumbar Injection of Alcohol

The paravertebral injection of absolute ethyl alcohol, or the so-called chemical sympathectomy, will not replace surgical sympathectomy. The injection can be only a substitute for operation. However, if the alcohol infiltrates the sympathetic ganglions, the destruction can give a comparable result to that of ganglionectomy.

The decision to perform an alcohol block is usually made when surgical sympathectomy is contraindicated because of the patient's general condition or when the

TABLE 5.—*Total Figures of Unilateral and Bilateral Paravertebral Alcohol Blocks of Lumbar Sympathetic Ganglions*

Anhidrosis Indicating Ganglions Blocked	Patients N.	Patients %	Blocks
Type 1 (L-1, L-2, L-3)	145	41.3	189
Type 2 (L-2, L-3)	82	23.4	105
Type 3 (unsatisfactory)	124	35.3	160
Total	351	100.0	454

operation is refused. Emergency paravertebral alcohol block of the lumbar sympathetic ganglions is indicated in some cases of acute arterial occlusion in the lower extremities owing to thrombosis or embolism, either alone or as an adjunct to embolectomy. It also may be of benefit in acute frostbite with involvement of the feet and lower part of the legs. However, block of appropriate sympathetic ganglions with alcohol

should be avoided if the patient has prothrombin deficiency from bishydroxycoumarin (Dicumarol) or allied drugs or prolonged coagulation time from heparin because of the danger of serious retroperitoneal bleeding.

The circulation in various arterial diseases can be improved in some instances by paravertebral blocking of the lumbar sympathetic ganglions, but we have not been impressed with the value of this procedure in cases of intermittent claudication. Of our 351 patients who had paravertebral injections of alcohol into the lumbar sympathetic ganglions, 97% had peripheral occlusive vascular disease (thromboangiitis obliterans or arteriosclerosis obliterans), and the rest (3%) had popliteal aneurysm, causalgia, and hyperhidrosis. The average age of the treated patients was 62 years; 74% of these patients were men.

Complications

Various complications of the paravertebral injection of alcohol, such as Brown-Séquard paralysis, regional neuritis, and neuralgia, have been observed. Review of the literature has revealed that neuritis developed after the paravertebral injection of alcohol in 10% of patients. It is obvious this complication occurs more frequently after blocking of the thoracic sympathetic ganglions and rami than of the lumbar ganglions and rami. The explanation is found in the close anatomic relationship between the sympathetic chain and the somatic nerves in the thoracic area. If paravertebral alcohol block of the thoracic sympathetic nerves is to be successful, the alcohol has to be placed close to the pleural surface into the sympathetic ganglions, and it is likely to reach the intercostal nerve. However, in the lumbar region, tissue and fat separate the sympathetic ganglions from the regional somatic nerves and prevent any immediate contact of these somatic nerves with the blocking agent. Should the alcohol, because of faulty technique or abnormal relationship of the sympathetic trunk with the somatic nerves, reach the latter, neuralgia or neuritis is likely to develop. The somatic nerve is paralyzed at first, but the anesthesia may disappear soon after the alcohol injection. Dysesthesia of the chest wall usually develops within a month. Lévy and Moore in their studies of the injection of alcohol into the thoracic sympathetic nerves reported intercostal neuritis of varying severity in 38 of their 45 patients (84%) and increased oral temperature, ranging from 99 to 104 F (37.2 to 40 C), for as long as four days after the block in 25 patients.

In our series of 351 patients with 454 paravertebral alcohol blocks of the lumbar sympathetic nerves, we did not observe any significant changes in oral temperature after the injection. Ten patients (3%) complained of mild pain at the site of injection, with extension into the buttocks or occasionally into the posterior aspect of the thigh. All these patients were given physical therapy, such as diathermy and massage; some were treated for as long as three weeks. The neuritis or neuralgia could be controlled easily by these measures, and no other complications were observed. One patient complained of mild backache six months after the alcohol block. All the others were dismissed and had no significant complaints referable to the injection of alcohol. In our opinion alcohol block under these circumstances is justifiable.

Summary

The effect of the paravertebral injection of alcohol into the lumbar sympathetic ganglions and rami was studied in 351 patients by means of the sweating test. Adequate sympathetic blocking with alcohol was achieved in 65% of all treated patients. Neuralgia occurred in 10 patients (3%) after the injection; this was controlled by physical therapy. Absolute ethyl alcohol is primarily used as a blocking agent at the Mayo Clinic.

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MILITARY MEDICINE—A SPECIALTY AND A CAREER

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There are two objectives to this paper. The first is to depict military medicine as a specialty, capable of being well defined as such, with a special body of knowledge, a special discipline of practice, special problems, and special solutions. This is done with the complete appreciation of the fact that within the scope of the military services today there is room, indeed there is imperative necessity, for all the recognized specialties as they exist in the civilian practice of medicine. But with this qualification plainly made, I believe that the concept of military medicine as a specialty is a sound one and its acceptance desirable.

The second objective is to demonstrate the advantages and opportunities for young doctors in this field. It is fondly hoped that some may thereby be persuaded to embrace this specialty as a career. Surely only when there is a large, dedicated, well-trained corps of career officers in this service can there be available the sort of medical care the armed forces expect and deserve. No more important contribution can be made to national security than the assurance of a healthy, well-adjusted, and happy defense force; and to this happy state, good medical care contributes greatly.

In a unique way the history of military medicine is the history of medicine itself. And, in fact, military medicine has made great contributions to medicine as a whole. One needs only to think of the treatment of wounds, the ligation of arteries, and the management of burns to realize the debt medicine as a whole owes to military medicine. Then, too, while it is recognized that great military operations on the modern scale are possible only because of the discoveries of medicine in the fields of hygiene and preventive medicine, it is precisely in these fields that the military has made great and

One needs only to think of the treatment of wounds, the ligation of arteries, and the management of burns to realize the debt medicine as a whole owes to military medicine. Great military campaigns on the modern scale are possible only because of the discoveries of medicine in the fields of hygiene and preventive medicine, to which military surgeons have made great and significant contributions, such as control of yellow fever and enteric disease and the conquest of scurvy, to name only a few. In modern times the management of injuries due to toxic gases and, more recently, to radiation has depended entirely on military sources. The recognition of these special services is important to the acceptance of the military surgeon as a specialist.

significant contributions, such as control of yellow fever and enteric disease, the conquest of scurvy, and the elimination of syphilis, to name only a few. And in modern times the management of injuries due to toxic gases and, more recently, to radiation injury has depended entirely on military sources. To list all of these contributions is for another more ambitious paper than this one. It is probably fair to say that the contributions of military surgeons to traumatic surgery, public health and preventive medicine, mass psychological problems, and nutrition are far ahead of what could reasonably be expected from the number of men involved. It does indicate, however, the pride the military surgeon can take in his career, and its appreciation should give to military medicine the prestige it deserves.

Chairman's address, read before the Section on Military Medicine at the 106th Annual Meeting of the American Medical Association, New York, June 4, 1957.

Military Medicine as a Specialty

To make the point that military medicine is a specialty and that it should be recognized as such requires that certain criteria be met. It must be shown that the alleged specialty deals with a special class of people, that the problems are of a special sort and call for special solution, and that special training and qualifications are needed in its practice. This demonstration will be attempted. In general the personnel coming under the care of the military surgeon (dependent care is another thing) are young, healthy adults, selected because they are free from disease and physical defects. They are being trained or are engaged in a special activity, namely, waging war. It is possible, without presuming to be comprehensive, to list certain special problems which arise from this situation.

Physical Standards.—The military has the opportunity, nay the obligation, to survey men and women on a vast scale as to their physical fitness and freedom from disease. The setting of standards of physical fitness and the devising of methods for physical examination and for the evaluation of findings is a special military problem—and one to which the military have made great contributions but have by no means solved. With the inclusion of special tests for aptitude and for mental stability, which are recent additions, great contributions can be made to civilian welfare by this form of military medicine.

Preventive Medicine.—The problem of preventive medicine in the military scene is certainly a special one, special in its manifestations, dealing as it does with men under special conditions of housing, transport, and exposure, but also special in its vital importance. Military operations on the modern scale would be impossible without it.

Mental Hygiene.—Nothing in human experience imposes such stresses upon the mind and nervous system as does the strain of battle. The preparation for this ordeal, the conditioning of the environment to make it tolerable, and the treatment of the inevitable consequences constitutes a problem almost uniquely special to military medicine.

Diet and Nutrition.—No other group in society is in the situation where all of its food is prescribed and provided with as little element of individual choice. The impositions of travel, combat, and supply are all special. The principles are of course biochemical and the same for all men, but the solutions call for special management and make this too a special military problem.

Military Casualties.—Casualties of war demand special solutions and special training and preparation. Only a few will be named: From the earliest days of the club, the pointed stick, the sword, and the spear through to gunpowder, military wounds have been different and special. Practically speaking, gas casualties are confined to military operations and all we know about them we have learned from the military surgeons. The new terrible problem of radiation injury is of course almost solely the product of military activity. Its solution may be vital for us all in the next war. Altitude effects are an outgrowth solely of military aviation and as such are special problems, as are all the problems of a similar origin such as effects of gravity, anoxia, pressure problems, cold adaptation, heat tolerance, dehydration, and many others, but these are enough to make the point of their being special military casualty problems. Shell shock and battle fatigue are serious and essentially special military problems.

This incomplete list lays the foundation for the fulfillment of the first criterion that the problems be special. It follows that the solutions are special too and that the training needed to apply them must be of a special sort. It would seem unnecessary to dwell tiresomely upon the justification of the notion that there is a specialty of military medicine. That the recognition of this concept is important to the acceptance of the military surgeon and to his prestige is not so well known as it should be. Everything proper should be done to give this branch of the profession the dignity and importance it deserves. The armed services and the country will be the ultimate beneficiaries of a better medical service. This improved service will be more attainable if proper recognition is given to the men engaged in it.

Military Medicine as a Career

If a case has been made for military medicine as a specialty, it would be proper at this time to point out why young physicians should go into it as a lifetime career. There are two principal factors in the choice of a lifetime career when this choice is deliberately made—material considerations and intangible motivations. The second are more important. First of all, a man who feels at all must feel that he is important, that the work he does has meaning for the benefit of mankind and for the advancement of the principles in which he believes, and in addition it helps greatly for most of us if our fellows respect us and regard our work as significant. For these reasons it is important that military medicine be important; that its importance in contributing to national welfare be recognized publicly and privately; that the opportunities for self-expression and for contribution to knowledge through research exist, and that their existence be pointed out to young physicians. Military medicine can and should offer unrivaled opportunities for a full, useful, professional career. Let this be known.

On the material side the young physician should be shown how the discrepancy between the income from practice and that in the services has lessened. The tremendous material advantages of the service in respect to job security, protection during incapacity due to illness, provision for retirement, opportunity for leave for study and recreation, and

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chances for travel should all be publicized. It is perfectly true that in a material sense the military medical man, while still in my opinion greatly underpaid, is not by any means badly off. It can be, as many can testify, a richly rewarding career. These facts should be made more generally known to young physicians at the time when they choose their life work.

Future of Military Medicine

There are few to whom is vouchsafed the gift of prophecy, and I am not one of these. But, as Heraclitus pointed out in 500 B. C., and which recent events amply corroborate, there is no certainty but change. Military medicine is changing and will change in the future. What these changes will be is not so much a matter of chance as it is the deliberate determination of men. And so it is not idle to speculate as to whither we should go, nor is it too presumptuous for any interested person to express himself as to what our proper objectives should be. I shall be presumptuous.

I believe military medicine should be developed as a recognized specialty and given all the prestige and importance that can be given to it. At the same time the recognition of specialization as it is presently understood should be furthered. One of the fine things since the last war has been the program for the training of specialists within the services and the increased opportunity given to specialists to function in the framework of military medicine. I would advocate the organization of military medical men as a component part of the American Medical Association with status similar to a state medical society and with duly and democratically elected delegates to the house of delegates proportional to the number of doctors in the military services.

I hope that the process of integration, already proceeding, will be hastened and that closer relationships between the three services, the U. S. Public Health Service, and the Veterans Administration be established and maintained. The field of research and investigation, already important, should be further cultivated, with ample opportunity provided for talented military medical men to exercise their talents in it.

I would like to see administration further relegated to medical administration and the number of trained medical men taken from medicine for administration kept as small as possible. I would even favor, as in the Navy program of "engineering only," that certain medical officers who desire this kind of activity—and some of this administration can only be done by doctors—so indicate early in their careers and be trained for this. It might be well to let rank be conferred to these men only (for command responsibility requires rank) and to have those who do medical work only be known as doctor and be paid for the jobs they occupy and not for the rank they hold. This, I realize, is a big step to take.

Finally, and in this I know there are many both in and out of the military who would dissent, I favor a military medical school in Washington for the training of potential military medical men.

This section has done much to advance the prestige of military medicine. Much more needs to be done. I want to pay particular tribute to Dr. Cecil Andrews to whom most of the credit is due for the fine program and to the whole-hearted support we have had from all three services and from the defense department. Let us continue to work for the advancement and recognition of military medicine.

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Disk Lesions and X-ray Films.—Lumbar backache is a common precursor of sciatica in cases of lower lumbar disk herniation; but this is insufficient evidence upon which to base the naïve assumption that any chronic or recurrent lumbar backache is due to a defect in the intervertebral disks. However, the fact is that in the minds of most doctors no tissue of the many in the back has quite the reality of the bones and their joints. One reason for this is that we look every day at photographs of the back which show nothing but the skeleton. If by some odd chance a "Y ray" or "Z ray" was discovered which showed only, for example, elastic tissue or collagen or tissue fluid, the bones being transiucent, and if we used it instead of X rays for a time, we should develop entirely new conceptions of the processes of disease in our patients. This is not to dismiss disk disturbance as a common cause of backache or even the usual one, but to question the worth of the evidence upon which it is so customarily assumed. . . . The X-ray film which demonstrates a return to normal alignment of a vertebral injury fails to reveal the mass of disk material which remains in the spinal canal and maintains a compression paraplegia. The X-ray picture cannot possibly exclude a disk prolapse. Plain X-ray films in all postures with the further aid of myelography may fail to discover any abnormality even in a case of the grossest severity. . . . Despite the presence of a damaging disk prolapse in the spinal canal, the intervertebral interval in the X-ray film may be quite normal.—W. S. Charlton, Whither the Disk? *The Medical Journal of Australia*, Dec. 8, 1956.

TRANSPORTATION OF SICK AND INJURED IN CIVILIAN AIRCRAFT

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Medical advice as to the transportation of patients in civilian aircraft is now based on an immense accumulation of experience. The year 1955 in the United States alone yielded data on more than 24 billion passenger-miles. Included were many passengers handicapped by various chronic defects, or going to medical centers for diagnosis, or returning home after treatment. The annual number of deaths during flight has ranged from 7 in 1948 to 20 in 1954; unconsciousness occurred 36 times in 1947 and 119 times in 1954. About half of the cases of unconsciousness or of death were ascribed to cardiovascular disease. Facts assembled on the incidence of motion sickness have led to concrete recommendations as to prevention and treatment. Certain patients should not fly without a companion well qualified to care for them in emergencies; certain others should not fly at all. For the vast majority of patients required to travel, however, flying is swift, comfortable, economical, and safe.

In daily increasing numbers the traffic and medical departments of the civilian airlines receive inquiries from patients and physicians as to the advisability of air travel.[1] There are many reasons for believing that sick and injured can be transported with greater speed, facility, and safety by air than by any other method.[2] Several authors have dealt at length with the medical contraindications for flight and have discussed extensively clinical and pathological conditions for which flying would be ill-advised.[3] All too often this has resulted in physicians counseling certain of their patients not to travel in civilian aircraft, thus denying them the advantages of swift, economical, comfortable, and safe transportation. This paper has been compiled through a literature survey and the submission of extensive questionnaires to the medical directors and vice-presidents of operations of the 56 certified commercial airlines and the operators of the 350 air ambulances now listed with the Civil Aeronautics Administration. Completed questionnaires and supplementary documents were received from 35 airlines (10 domestic trunk airlines, 9 international airlines, and 16 local service airlines) and 45 air-ambulance operators.[1]

In the early development of the civilian airline industry, the rule of thumb "those who can walk, may fly" was often applied, and a ticket was sold to any passenger who could pass the "look normal, walk normal, act normal, talk normal, smell normal" test.[1] Currently the Air Transport Association of America regulations state:

> Carriers will refuse to carry, or will remove en route, any passenger whose status, age, physical or mental condition is such, in the opinion of the carrier, as to:
>
> 1. render him incapable of caring for himself without assistance unless
>   a) he is accompanied by an attendant who will be responsible for caring for him en route
>   b) with the care of such attendant, he will require no more attention and assistance from employees of the carrier than an ordinary able-bodied passenger
> 2. render him objectionable to other passengers
> 3. involve hazard or risk to himself or other persons or to property.[4]

Since airlines are common carriers, passengers will be accepted regardless of race, color, or creed. Although few absolute exceptions to flight are made by the carriers, they will generally not carry intoxicated passengers, passengers with known, serious infections or contagious diseases, psychotic or mentally incapacitated patients, patients in body respirators, women in active labor, comatose patients, or passengers with severe skin rashes or cyanosis. Passenger selection is generally made by the senior ticket agent or station manager; however, in all cases, the captain of the flight has the final authority as to who may fly. For most carriers the policy determining which patients may fly represents a compromise between compassion to the sick and injured and their families and the responsibility to other passengers for safe, comfortable, and enjoyable flights.[1]

Armstrong[5] has recently stated that 3% of the regular airline passengers are ambulatory patients. During 1955 the American scheduled airlines flew 41,623,000 passengers over 24,338,000,000 passenger miles in 1,688 daily scheduled flights, utilizing 1,955 separate aircraft.[6] This total number, including passengers of all age groups (of whom two-thirds were male), constituted 33% of all intercity passenger-mile market within the United States. As an interesting side light, in a recent survey of June, 1956, it was found that of all passengers traveling between the North American continent and Europe more than 50% traveled by air.[6] This total passenger load was carried with an accident fatality rate of less than one per 100 million passenger miles.

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Most patients flying in commercial aircraft will fall into one of the following four categories:[7] (1) patients on their way to metropolitan area diagnostic and therapeutic clinics and hospitals, (2) convalescent patients returning home after therapy, (3) ambulatory patients with minimal pathology, flying in the course of their normal business and social activities, and (4) those terminally ill, traveling to be with relatives at the time of death.

Physiological Aspects of Flight

For medical purposes all airline passengers can be divided into three groups:[8] (1) those apparently well, (2) those with physiological deviation from normal with respect to air travel without pathological processes being present (such as pregnancy, early infancy, and congenital malformation), and (3) those apparently not well. Discussion of these three groups hinges on the major differences between surface travel and flight, i. e., irregular movements of the plane due to turbulence, decrease in total barometric pressure, and absolute decrease of the partial pressure of oxygen delivered to the lungs.

Air-sickness, the most common physiological disturbance associated with flight, is closely tied to turbulence. It is thought that the angular accelerations due to motion of the aircraft are the primary cause of motion sickness, but the underlying factors of anxiety, apprehension, and fear are strong predisposing influences. To many commercial passengers, flying seems more dangerous than it really is due primarily to lack of information on accident rate, the wide publicity usually given by the press concerning aircraft accidents, and confusion between military and commercial operations. Patients are usually more susceptible to develop motion sickness than are able-bodied passengers, and women and children are much more susceptible than adult males.[8] It has been found that visual orientation is an important sensitizing factor and that a higher incidence of motion sickness is encountered during daylight hours than at night. Since most aerial maneuvers are to the left, avoidance of the left window seats and flying with the seat at the reclining position will diminish the incidence. Assurance by the physician and premedication with anti-motion-sickness drugs greatly minimize the incidence of this condition.

Lederer [9] has stated, after careful evaluation of many anti-motion-sickness preparations, that the best prophylactic and therapeutic agents now available are cyclizine (Marezine) hydrochloride, 50-mg. tablet, and meclizine (Bonamine) hydrochloride, 25-mg. tablet or chewing tablets (gum). For children 6 to 10 years of age one-half the dose is given, and for children under 6 years of age one-fourth the adult dose for either drug. Cyclizine is less apt to cause drowsiness than any other remedy. Its effect is almost instantaneous, and its therapeutic effect will last approximately four hours. It should be taken prophylactically 20 to 30 minutes before take-off. Meclizine is more apt to cause drowsiness, but its effects will last approximately 24 hours. The same conclusions were reached by the Army, Navy, and Air Force Motion Sickness Team in a study of 16,920 soldiers and airmen crossing the Atlantic.[10] Prophylactic measures such as no preflight alcohol ingestion and a light preflight meal are also efficacious. Resistance to the development of air sickness greatly increases with age and travel experience. Pressurization systems and higher wing loads have made it possible for aircraft to fly at higher altitudes, thus avoiding much of the turbulence. Not all aircraft are pressurized, nor is it necessary on low-altitude flights, but more and more modern transports have pressurization systems which maintain passenger compartment altitudes at or below 10,000 ft. regardless of flight altitude.[1] Pressurization gives the advantages of comparatively slow ascent and descent of the passenger compartment, minimizes the change in total atmospheric pressure, and makes oxygen unnecessary in flight on an individual basis.

The group of passengers apparently well needs no discussion. Of the physiological deviations from normal, let us first consider pregnancy. The following policy is recommended by the Airline Medical Directors Association.[7]

> Any woman in a pregnant condition shall be accepted from the beginning of the first month on through to the end of the eighth month of gestation without question. Any woman in the ninth or last month of pregnancy shall be accepted who can furnish a certificate from an obstetrician dated within 72 hours of departure stating that he has examined and found her to be physically fit for transportation from (place) to (place) on (date) and that the estimated time for the birth of the baby is (date).

Women in late stages of pregnancy should, if possible, select seats facing the rear, so that the safety belt may be worn rather loosely over the legs and under the fetal abdominal bulge. In-flight oxygen may be advisable for those with mild dyspnea due to the increased abdominal pressure with resultant limitation of respiration. It is not unusual for those near term to develop false labor contractions within 24 hours after descent, and any patient traveling in the later stages of pregnancy should be warned that this may occur.[1] Webb and Harvey [11] have concluded, from their own statistical study of the effects of travel by air or surface on pregnant military dependents and from a review of the previous studies by Beach, Diddle, Mackie, Whittingham, Guilbeau, and Turner, that travel by present-day means (aircraft included), with judicious use of common sense, is without harmful effect on a normal pregnancy regardless of the duration of the pregnancy. I know of no reliable report of deleterious effect to the unborn child or mother due to premature labor or anoxemia at altitude on a commercial aircraft.

Infants less than 10 days of age should not be transported by air for any great distance, as their respiratory mechanisms are not yet sufficiently established to permit the infant to be exposed to a respiratory stress situation.[8] Beyond this age, however, babies with a normal cardiorespiratory system have an advantage over adults, since it is well known that infants tolerate hypoxia better than adults. The wide range of congenital malformations must be considered on an individual basis. Congenital heart conditions and lung atresia are not ordinarily contraindictions to flight. If the individual is ambulatory and is able to climb one flight of stairs, ordinary flying is permissible. Individuals limited in activity may fly, provided therapeutic levels of oxygen are provided before flight is undertaken.

TABLE 1.—*Comparative Volume of Gastrointestinal Gases and Percentage of Oxygen Saturation of Arterial Blood at Various Altitudes**

Altitude, Ft.	Relative Body Gas Volume	% Arterial O_2 Saturation
Sea level	1.0	96
5,000	1.2	92
10,000	1.5	88
15,000	1.9	80

* Data from Armstrong, H. G.: Principles and Practice of Aviation Medicine, ed. 3, Baltimore, Williams & Wilkins Company, 1952.

Other Medical Considerations

Next let us consider patients with cardiorespiratory disease. For those with valvular heart disease, angina pectoris, hypertension, asthma, and pulmonary tumors, the certified airlines have available on almost every flight, either free of charge or at small cost to the passenger, oxygen delivered through nasal or oral masks.[1] These systems may be adjusted to deliver oxygen-enriched ambient air or 100% oxygen. As air transportation becomes more common, the anxiety formerly encountered frequently on commercial liners has become much less of a problem. Preflight sedation and reassurance by the physician will greatly add to the in-flight comfort of these patients. Although the pressurization systems will maintain a cabin altitude of 10,000 ft. or below, trapped gases within body cavities will still expand to approximately one to five times their volume at ground level. For this reason it is believed that patients with spontaneous or therapeutic pneumothorax, mediastinal or subcutaneous emphysema, infections by gas-forming bacteria, and any of the large group of diseases which have as part of their make-up trapped gases within body cavities, should not fly.

TABLE 2.—*In-flight Injury, Unconsciousness, and Death on American Scheduled Airlines**

Type of Incident	Year							
	1947	1948	1949	1950	1951	1952	1953	1954	1955
Unconsciousness	36	67	63	85	83	89	117	119	88
Death	14	7	9	13	10	16	17	20	18
Injury	..	..	..	..	22	12	10	13	5

* Data from reference 13.

Two other clinical conditions which may result during flight are aerotitis and aerosinusitis resulting from improper ventilation of the middle ear or sinuses during descent from altitude. They are caused by tissue edema resulting from upper respiratory infections or lymphoid blockage of eustachian tube and sinus orifices and by failure to "clear" these cavities during descent. The incidence of these conditions can be greatly reduced by use of nasal vasoconstrictors, by staying awake during the letdown and landing phases of flight, by chewing gum or eating candy, by swallowing frequently, or by doing a mild Valsalva maneuver. Nursing infants should be offered the bottle or breast during descent to assist in keeping the eustachian tube orifices open by oral pharynx muscular contractions.

Most carriers [1] will allow a blind passenger's seeing-eye dog to travel in the passenger compartment if properly muzzled and secured on a short leash. Wheel-chair patients will be carried in most circumstances if prior arrangements are made for assistance to the passenger during loading and deplaning activities. If prior arrangements are made, many carriers will transport litter patients either on the standard canvas stretcher or on litters specially designed for the specific aircraft, which are available through the traffic department. Patients wearing plaster casts will be transported if the casts are not of such size or shape as to prevent the passenger from being accommodated by the regulation seat. Patients whose mandibles are fixed, either by jaw wiring or head traction, are not advised to fly commercially due to the possibility of air sickness and aspiration of vomitus. However, I, as well as other physicians experienced in the air evacuation of military patients, have had considerable success in flying persons whose mandibles are fixed with safety by use of the blunted hypodermic needle "rip cord" method of fixation developed by Traeger.[12] In this system all wires loop around hypodermic needles, one on each side of the mouth. With only slight traction, these needles pull free, permitting the patient to open his mouth to vomit if necessary. Colostomy patients should be advised

TABLE 3.—*Example of Certificate of Release from Responsibility*

I, ..., do hereby release Any Airlines Incorporated from any and all responsibility for injury or illness incurred as a direct or indirect result of my admitted ..... condition while boarding, flying in, or deplaning from the aircraft designated as Any Airlines Incorporated flight ..... on this ..... day of ....., 19..... from ..... to ..... I further state that my condition is not contagious and I will not require any assistance from, or medical treatment by, Any Airlines Incorporated personnel en route.

.....
Signature

Accepted by: .....
Street Address

....
Representative City State

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that their bags will expand somewhat in flight due to the pressure change. Tracheotomy patients will be transported so long as they do not require suction. Patients with diabetes mellitus may fly if they can give themselves their own insulin or will need no insulin in flight. However, those near diabetic coma or subject to sudden insulin shock should not fly. Epilepsy has a tendency to manifest itself at altitude, especially in nonpressurized aircraft, due to anxiety, hyperventilation, and very mild hypoxia. Moderately heavy preflight sedation, reassurance, and proper oxygenation during flight will usually permit them to fly satisfactorily. Epileptics subject to frequent seizures should travel with a companion when possible.

TABLE 4.—*Example of Medical Release*

I, John Doe, M.D., being duly registered and licensed in the State of Florida, certify that in my opinion, the health and physical condition of:

Mr. Jim Jones

whom I have recently examined, is such that he/she can fly from _____ to _____ as a passenger, without risk to others or to himself/herself and without the requirement of more attention from those engaged in operating the plane or attending its passengers than is ordinarily required by an average passenger, under the following conditions:

Check one: [1. Can fly when accompanied by Registered Nurse as attendant.
2. Can fly unaccompanied.

The patient's condition is such that there should be no lapse of consciousness or tendency to become nauseated. The patient will not require treatment employing the use of apparatus. The patient's condition is such that irregular flight operations, a flight of greater length than the published schedule, or a flight terminating at a point other than the patient's expected destination will not involve risk to the patient.

Signed John Doe

Address 1639 Collins Ave., Miami Beach, Fla.

Date July 9, 1956

I understand that if necessary for the comfort of other passengers, or upon competent medical advice, Any Air Lines, Inc. may refuse passage or remove me at any point and refund the appropriate portion of my fare without further obligation.

Signed Jim Jones

Passenger

The airline stewardesses, although no longer required to be registered nurses, are well trained in first aid and carry as part of their in-flight equipment bandages, splints, aspirin, bufferin, aromatic ammonia spirits (smelling salts), anti-motion-sickness drugs, glyceryl trinitrate, and padded tongue blades for passengers who have convulsions.

Data on in-flight injury, unconsciousness, and death on scheduled domestic air carriers between 1947 and 1955 are summarized in table 2.[13] Approximately 25% of all in-flight deaths and incidents of unconsciousness were associated with previously existing illnesses or disabilities. Of the deaths for which a cause is reported, about 50% were due to cardiovascular disease. The frequently reported causes of unconsciousness were cardiovascular disease, epilepsy or epileptiform conditions, recent emotional stress, anxiety states, fatigue, and motion sickness. The majority of fatal incidents occurred while passengers were in their seats. Mortality rates were about equal for men and women, but women became unconscious three times more frequently. Injuries reported were in almost every case minor and, with one exception, due to turbulence of the aircraft.

The 350 air ambulances are distributed geographically about the United States, with most planes per population unit in the great plains and the southwestern states, and are generally one-or-two-engine, two-to-five-place aircraft. Patients with acute surgical emergencies comprise a large percentage of those carried by these aircraft, and the operators make very few exceptions as to which passenger may fly, generally accepting anyone recommended by a physician and carrying a physician's certificate.[1] All aircraft used in these operations are licensed by the Civil Aeronautics Association and have met specific air-worthiness standards. They are generally equipped with one or two litters, in-flight oxygen, bedpans, urinals, emesis basins, blankets, pillows, sheets, and, in many cases, in-flight suction apparatus. They perform an extremely valuable service in transporting patients from isolated or rural areas to metropolitan diagnostic and therapeutic centers.

The comfort and safety of passengers in flight will be greatly enhanced if the physician will furnish a medical certificate to the ticket agent and a letter to the flight stewardess outlining generally the patient's condition and such attention as may be needed during the trip. Passengers should be advised to arrive at the airport well in advance of take-off time so that they may be loaded in the most desirable seats for their condition prior to the loading of the other passengers. In general, night or early morning flights will be much less turbulent than those during midday or afternoon.

Due consideration of the total distance to be traveled, elapsed travel time, and whether the patient would have to travel by some other means will often make obvious the decision as to whether or not flight should be undertaken for any individual patient. With modern aircraft equipment for pressurization, ventilation, and temperature and humidity control, the commercial airliner approaches very closely the comfort of the patient's own living room. For the vast majority of patients required to travel, modern aircraft offers swift, comfortable, economical, and safe transportation.

287 E. North Broadway (14).

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PSYCHOSOMATIC ASPECTS OF ALLERGY IN CHILDHOOD

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The author's experience with allergy in children has fortified his belief that allergic illnesses in childhood have a basic immunological etiology. Early recognition of the allergic state, thorough and careful allergic diagnostic study with adequate treatment, both therapeutically and prophylactically, insures a good result in most children with allergic illness. If such illnesses fail to respond to medical management, the child's physical and psychological environment must be more deeply evaluated. Separation of the child from his usual surroundings, particularly his parents, for periods of 6 to 12 months has given results that were rewarding for the greater number of children. The influence of maternal rejection, fear of separation from the mother, and other forms of unhappiness in the home environment is recognized, but the patient also deserves the relief he might obtain from an allergic investigation, immunization, and medication.

Today, as many of us know from actual experience in private practice, the greater number of children with allergic illness of short duration respond readily when treated on a strictly allergenic basis. Their allergic illness is most often caused by allergenic substances to which they are sensitive. There is, however, a small, vocal minority of physicians who have attempted to seed both the medical and lay minds with the thought that all allergic symptoms are primarily induced by psychological imbalance. Specifically with reference to asthma, some physicians have claimed that psychological influences may play the significant role in causing attacks of asthma for the first time in many patients. Claims on the part of some psychiatrists and allergists that disturbances of an emotional nature may give rise secondarily to repeated episodes of asthma are generally accepted. Few physicians concerned with the treatment of allergic diseases would deny that emotional disturbances are in some way related to this group of illnesses. However, many competent physicians seriously question the sweeping generalization that asthma arises primarily in mentally disturbed individuals.

From the Children's Allergy Clinic, Pediatric Service, the Mount Sinai Hospital.

Read in the Session on Allergy before the Section on Miscellaneous Topics at the 106th Annual Meeting of the American Medical Association, New York, June 5, 1957.

Parent-Child Relationship

Weiss [1] postulated, in 1922, that the asthmatic attack is caused by fear of separation from the mother. French and others [2] studied 11 asthmatic

children—6 boys and 5 girls—at the Chicago Institute for Psychoanalysis. They revealed that only five of this group remained in analysis for as long as six months. The patients showed a common pattern. Their attacks of asthma were considered to be equivalent to a suppressed cry for the mother whom the patient is in danger of losing. Situations which threaten to separate the patient from the mother or mother-figure tend to precipitate attacks. Moreover, these situations usually result from some temptation to which the child is exposed. Asthma is expressed as part of a defense mechanism. From the analytic material, the writers feel that the fear of separation from the mother is a primary etiological factor and not merely a secondary reaction to the attack itself. The study of such a small group over a period of only six months without adequate controls is hardly conclusive. The authors admit to the theoretical nature of much of their data. Their contributions have been evaluated as being thoughtful and stimulating, but the material presented and the conclusion derived from this group is unsatisfactory.

Subsequently, Miller and Baruch [3] published a series of papers in which the mother-child relationship was explored in allergic, particularly asthmatic, children. They reported that maternal rejection was established in 98% of a group of allergic children, whereas, in a control group of psychologically disturbed nonallergic children, only 24% revealed evidence of significant maternal rejection. Marked differences in expression of hostility were found to exist between these two groups of children. Eighty-three per cent of the nonallergic or control group of disturbed children expressed open hostility toward the parent or parents, while only 20% of the allergic children could do this. They theorized that the allergic child is rejected by his mother and, because he is unable to express his hostility toward her, he often turns it inward upon himself; the asthmatic attack results from the conflict produced in him by his rejecting mother.

Despite this statistical evaluation by Miller and Baruch, their conclusions have been questioned because of the largely subjective nature of the material, which depends upon the interpretation of play and the assumptions that certain behavior is linked with certain emotions and that asthmatic attacks are causally related to the particular mother-child relationship. Two significant definitions of "maternal rejection" have been offered us. Newell [4] defined it as "that situation where the birth of the child was unwelcome to the mother." More broadly, Figge [5] said that a "rejecting mother is one whose behavior toward the child is such that she consciously or unconsciously has a desire to be free from the child and considers it a burden."

Jessner and associates,[6] in a psychoanalytic study of asthmatic children, emphasized the importance of the emotional impact of nearness and separation for the asthmatic child and its mother. They stress the paradox of the mother clinging to her child and pushing it brusquely away toward premature independence, which can be understood only in terms of the mother's unconscious need and her defense against it. They agree with Miller and Baruch's concept of maternal rejection but describe this as only one aspect of a complex relationship.

The fallacy of the maternal rejection theory has been noted by two prominent psychiatrists, Levy [7] and Ziskind,[8] who have commented that, in itself, maternal rejection is a universal characteristic of our society. All of us have been accepted and rejected by our parents at different times. Although Ziskind feels that the problem becomes one of quantitative evaluation to indicate at what point this universal experience becomes a pathogenic or critical factor, there are no quantitative means available for accurately measuring these phenomena.

Defense Reactions

Wolf,[9] in 1950, supposed that the allergic reaction of the upper respiratory tree is a defensive one of shutting out (bronchospasm) and washing away (excretion). Abramson,[10] recently, on the basis of psychoanalytic studies of allergic individuals, postulated the syndrome of engulfing parents and suggested the term "Cronus complex" for it. He feels that the theory of maternal rejection often not only is incomplete but may frequently be misleading in the attempt to understand and treat the severe and protracted allergic manifestations in children and adults. He holds that in some cases where the allergic process persists, as in severe eczema or uncontrollable asthma, the disturbance in the parent-child relationship is not parental rejection but rather mutual engulfment or introjection. Rejection subsequently may ensue when mutual engulfment fails to satisfy the parent's needs. Rejection is not limited to the maternal parent but may also or only involve the paternal figure, and, even then, rejection need not be manifest in all areas.

Bacon [11] recently theorized that asthma caused by a neurosis is a response to unconscious fears of assault upon the respiratory apparatus, and the physiological changes that accompany it are attempts to ward off that assault. She theorizes that aggressive excretory fantasies, stimulating the excretory mucosae (including the genital), may reflexly stimulate or sensitize the respiratory tract. When the respiratory tract has been thus sensitized, asthma can be precipitated by aggression from a punitive superego or from an environmental equivalent.

Treatment

Some 25 years ago, it was recognized that, in many cases, children with severe, intractable asthma were more effectively treated away from their home surroundings. The deleterious relationship of a disturbed, tense, and unhappy home environment on children who have protracted, severe asthma was

emphasized. The term "parentectomy," denoting the need of separating these chronically ill children from their parents, was coined by Peshkin.[12] Subsequently, a home in Denver was established to provide long-term care for these children. Many of these chronically incapacitated children have spent two to three years at the home and have returned vastly improved.

The practicing psychiatrist and the "orthodox" allergist fail to understand each other. The word psychiatry and the prejudice aroused by it, as well as the difficulties of language, methodology, and excessive claims, all contribute to the misunderstanding in these areas of discipline.

The personality structure of allergic children has been charted to demonstrate (1) a neurotic type of personality, (2) a high intelligence on verbal tests with poorer performance ability, (3) a marked overanxiety and lack of self-confidence, (4) a considerable latent aggressiveness and egocentricity, and (5) a compulsive type of personality with exaggerated orderliness and cleanliness. One group of investigators established that the single feature common to the personalities of asthmatic children was a deep-seated insecurity and a varyingly intense need for parental love and protection. Another study established that immaturity of behavior, seclusiveness, and moodiness with depression as the predominant mood were characteristics of the asthmatic children as a group. Thus the attempt has been made to describe accurately the personality of the child who has asthma. But despite this aggregate of words, there emerges no clear picture of a particular type of personality structure.[13]

Continued and detailed study of many children in the past decade, both in private practice as well as in an institutional setting, has fortified my belief that allergic illnesses in childhood have a basic immunological etiology. Awareness of this significant fact is of major importance, for treatment directed on this level gives excellent results in the majority of children. Early recognition of the allergic state and thorough and careful allergic diagnostic study with adequate treatment both therapeutically and prophylactically insures a good result in most children with allergic illness. When the persistent allergic condition fails to respond to adequate and competent allergic management, in other words, when allergy becomes chronic, then the child's environment, consisting of both physical and mental factors, must be more deeply evaluated. However, often it becomes necessary to enforce separation of the child from his surroundings. My own program for severely asthmatic children was established in 1953 at the Loeb Home, Eastview, N. Y., 40 miles from New York City, where children have spent periods of from six months to one year, and the results achieved were rewarding for the greater number of children.

This program substantiates in essence the importance of removing from their parents severely ill asthmatic children who have failed to respond to competent allergic management. Thus, the emotional stresses or barricades erected by both parents and child, which interfere with the patient's getting well, are minimized or reduced. Investigations of their allergic status and subsequent treatment may follow during this separation. Experiences with many of these chronically ill children during their interim "sabbatical" permits adequate allergic survey and management and, in addition, the opportunity "to study the effects of mental weather upon the ramparts of the body." [14]

It is well to recall the fact that within the narrow confines of one's body there is a very close reciprocal relationship between soma and psyche. The patient deserves the relief he might obtain from an allergic investigation, immunization, and medication. The focusing of his attention only on the emotional factors in his illness may direct the patient away from adequate medical treatment.[15] Frequently, parents will run from a physician who consciously or unconsciously points out an unsuitable parent-child relationship, and they are, as Abramson [16] has so clearly pointed out, both consciously and unconsciously grateful to the physician who studies the child's allergic symptoms on a strictly physical basis. These protracted allergic problems in children are basically immunological, but, during the course of treatment, if these immunological problems are inadequately resolved, then psychological disturbances secondarily intervene and may distort the entire presenting picture. The allergic child is no different from any other child with a chronic illness. Combined attention to the whole individual—body and mind—produces better therapeutic results than attention solely to either one or the other.

16 E. 79th St.

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EFFICACY OF URETHRAL CATHETERIZATION FOR DETERMINATION OF URINARY TRACT INFECTION

RESULTS WITH A NEW TECHNIQUE

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and
Paul S. Rhoads, M.D., Chicago

It is extremely important to differentiate between causative micro-organisms in urinary infection and those which are merely contaminants. Despite meticulous preparation of the urethral meatus and surrounding surface, the anterior part of the urethra retains its "normal" flora. A technique is presented to prevent or at least lessen the risk of contamination in obtaining a bladder urine culture.

In many instances of positive cultures from bladder urine obtained in the usual manner, there is uncertainty as to whether the micro-organisms found are the causative ones in an actual urinary infection or are merely contaminants. The importance of contamination in urethral catheterizations has been clearly shown by Guze and Beeson,[1] who obtained urine specimens from women by direct needle aspiration of the bladder at laparotomy and shortly afterward obtained a second specimen in the operating room by catheterization. Of the 12 urine specimens obtained by each method, those obtained by needle aspiration were all sterile, whereas the catheterized specimens had growth in four of the cases. They also cultured the tip of the urethral catheter after having inserted it into the urethra of women who had been prepared in the operating room and found micro-organisms in 6 of the 13 cases. It appears, therefore, that, although the urethral meatus and surrounding surface may be rendered more or less sterile, depending upon the thoroughness of cleansing, the anterior part of the urethra itself retains its "normal" flora. A catheter introduced into the bladder must pass through this flora.

In an effort to obviate this difficulty, a technique was conceived that made use of a catheter within a catheter and allowed the separate collection of bladder urine obtained through each catheter for the purpose of comparison. It was thought that in this way the inner catheter would be shielded by the outer one and therefore would be less apt to become contaminated. The insertion of the outer catheter into the urethra and bladder would not differ essentially from the technique usually employed in obtaining bladder urine.

From the departments of medicine, Chicago Wesley Memorial Hospital and Northwestern University School of Medicine.

Read before the regional meeting of the American College of Physicians, Champaign, Ill., Oct. 12, 1957.

Method

The study was limited to female patients who required catheterization for any reason, usually on the suspicion of a urinary tract infection. Some of the patients were known to have cystitis or pyelitis. Males were not included for the reason that in them a "clean voided" specimen is usually obtained for culture. Also, patients were not used who had received any antibacterial drugs within the previous 48 hours. A total of 45 catheterizations in 38 patients makes up the study.

A no. 20 rubber catheter was used for the outer catheter. Since this has a side perforation near the tip, the tip was cut off in order to allow the inner

catheter to come out straight instead of at an angle. The inserting end was then tapered to facilitate insertion into the urethra. The catheters are shown in figure 1 and their positions in the urethra and bladder are represented diagrammatically in figure 2. The inner catheter was an unchanged no. 8 rubber catheter.

Fig. 1.—Outer and inner catheters used to obtain specimens of bladder urine for culture.

Both hands were gloved, and, after thorough cleansing of the vulva with soap sponges followed by cleansing with sponges soaked with benzalkonium (Zephiran) chloride, the labia minora were spread apart with the fingers of the left hand, and the outer catheter was inserted into the urethra a distance of 2 cm. This is normally short of the bladder by 1 to 2 cm. The outer catheter was then held in place by the left hand shielded by sterile gauze while with the right hand the inner catheter was inserted into the outer one and pushed through it as far as the bladder, to the point at which urine was obtained. While an assistant held the sterile centrifuge tubes (which were supplied with cotton stoppers), two specimens were obtained; the inner catheter was then withdrawn and its tip dipped into a tube of tryptose phosphate broth, with use of aseptic technique. The outer catheter was

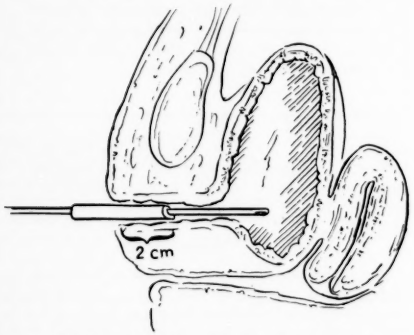

Fig. 2.—Catheters in place, the outer one 2 cm. into the urethra and the inner one into the bladder.

then advanced as far as the bladder, and two specimens were obtained through it. The outer catheter tip was cultured in the same way as the inner one.

Of each pair of urine specimens, one was used for a routine urinalysis and a Gram stain was made of the centrifuged sediment. The other specimen was centrifuged for 10 minutes, the supernatant urine was poured off, and tryptose phosphate broth was added in an amount equal to the original volume. The two urine cultures thus prepared and the catheter-tip cultures were then incubated at 37 C for a period of 96 hours before being considered negative. As soon as any growth became apparent in the tubes, streak cultures were made on heart infusion agar containing 10% defibrinated sheep cells and Levine's eosin–methylene blue agar for further identification of the micro-organisms. Fermentation studies were done in addition when necessary.

Results

There were 42 urine culture specimens obtained through the outer catheter, of which 22 (52%) were positive. Of 41 urine culture specimens obtained

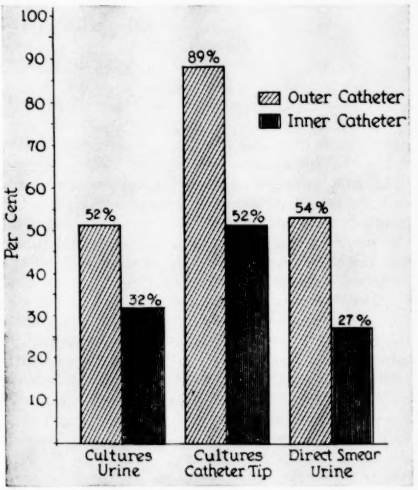

Fig. 3.—Frequency of positive cultures and direct smears in outer and inner catheter specimens.

through the inner catheter, 13 (32%) were positive. The tip of the outer catheter had micro-organisms in 39 of the 44 catheterizations (89%), and the tip of the inner catheter had micro-organisms in 23 of 44 catheterizations (52%). Smears were obtained of the outer catheter urine in 37 cases, and of these 20 (54%) were positive. Smears of inner catheter urine were obtained in 33 cases and were positive in 9 (27%). These results are represented in figure 3.

Of the 40 catheterizations in which both outer and inner catheter urine cultures were obtained, in 11 (27%) the outer catheter specimen contained a micro-organism not also present in the inner catheter specimen. On the other hand, in only one of the 40 cathe-

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terizations was a micro-organism present in the inner catheter urine that was absent from the outer catheter specimen.

Of 44 catheterizations in which the tips of both outer and inner catheters were cultured, in 26 (59%) a micro-organism was present on the outer catheter and not on the inner one. In 9 of the 44 catheterizations the reverse was true (20%).

Both outer and inner catheter urine smears were obtained in 30 catheterizations. In five the "outer" smear was positive while the "inner" was negative, and in one instance the reverse was true. In the remaining 24 catheterizations there was no difference between the two smears.

The percentage of catheterizations showing a difference in urine culture, catheter-tip culture, and urine smear is shown in figure 4. There were five

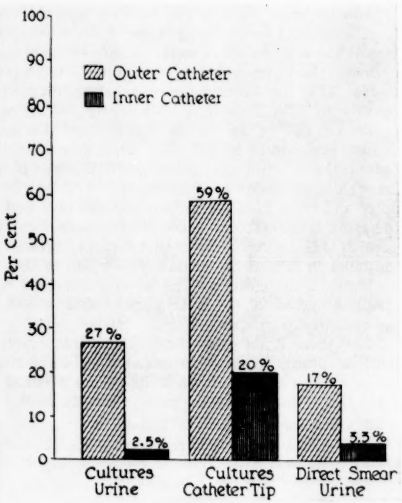

Fig. 4.—Percentage of catheterizations in which there was a bacterial species present in the outer catheter specimen absent from the inner and the reverse.

catheterizations in which the outer catheter urine smear was positive and the corresponding urine culture or both the urine culture and the catheter-tip culture were negative.

The micro-organism most frequently encountered was Micrococcus (Staphylococcus) pyogenes var. albus, and it occurred in the outer catheter cultures (urine and catheter tip) twice as often as in the inner catheter cultures. Second in frequency were coliform bacilli, which were only slightly more frequent in the outer catheter cultures than in the inner, the relative frequency being 7:5 in the urine cultures and 7:6 in the catheter tip cultures. Bacilli of the Proteus group appeared five times in the outer catheter-tip cultures but only twice in the inner, and were present only once in the urine culture (both outer and inner). Other micro-organisms were recovered infrequently, no one occurring in more than three catheterizations.

Comment

The results obtained show a decided difference between the two culture series with respect to percentage of positive findings, that is, positive urine cultures were obtained in 52% in the outer catheter series as compared to 32% in the inner, and positive outer catheter-tip cultures were obtained in 89% as compared to 52% positive in the inner. Hundley and coworkers [2] catheterized 50 normal nonpregnant females and obtained positive cultures in 44%. Marple [3] catheterized 100 unselected patients from a women's medical ward using a glass catheter after preparing the urethral orifice area with boric acid and merbromin (Mercurochrome) and obtained positive cultures in 31%. If it is remembered that our series consists of patients in whom there was at least the suspicion of a urinary tract infection and of a few with known infections, a higher percentage of positive results is to be expected. Even so, the finding of positive urine cultures in 32% in the inner catheter series is very close to the percentage obtained by Marple in 100 unselected cases and suggests some effect of protection against contamination in our series.

The 89% positive outer catheter-tip cultures is higher than the frequency obtained by Guze and Beeson.[1] Their catheterizations were carried out in the operating room under optimal conditions for aseptic technique. The conditions of our catheterizations were the same as those of the standard technique of catheterization on the ward. Whether this is adequate to explain our higher frequency of positive catheter-tip cultures cannot be stated. The frequency is much lower in the inner catheter-tip culture series (52%).

The direct smear results are consistent with the culture results in showing a higher percentage of positive findings in the outer catheter series. However, they are not considered to be as sensitive for purposes of comparison as the cultures, since in cultures that are allowed to incubate for 96 hours there is no difficulty in distinguishing positive and negative results, but where there are only a few micro-organisms in a smear these might well be missed.

The preponderance of positive cultures in the outer catheter series appears to be irrespective of the type of micro-organism, although in the case of coliform bacilli the difference was small. Most of the patients in whom coliform bacilli were recovered in the urine were considered prior to the catheterization to have a urinary tract infection, and in these patients all specimens were positive for coliform bacilli.

The relative frequency of the various micro-organisms is different from that obtained by one of us and co-workers,[4] who found Escherichia coli the most fre-

quent micro-organism in the urine of 325 patients studied, with Streptococcus faecalis and Pseudomonas aeruginosa next in frequency. The present study, however, is much smaller and also is limited to female patients, whereas in the larger series both sexes were included. Also, the previous study was limited to patients considered to have established urinary tract infections, while in the present study the majority of patients were free of symptoms. The indication for catheterization in the present study usually was the presence of more than 8 to 10 leukocytes in a urine specimen taken after a vaginal douche. The greater differential between outer and inner catheter specimens in the case of micrococci than in the case of coliform micro-organisms supports the impression that most often micrococci are contaminants from the urethra.

When a count is made of the individual catheterizations that show a micro-organism present in one set of specimens not present in the other, the contrast becomes even more marked: in 27% the micro-organism was present in the outer catheter urine only and in 2.5% it was present in the inner catheter urine only; for the catheter-tip cultures the respective values were 59% against 20%. This last figure seems high. In certain instances it is possible that the micro-organism failed to grow in the outer catheter-tip culture because of the presence of other micro-organisms that inhibited its growth. In other instances it is probable that the inner catheter tip became contaminated through faulty technique from some source other than the outer catheter or the urinary tract. An effort was made to avoid contamination, but at the same time we endeavored to keep the procedure as simple as possible and as unencumbered as the usual catheterization procedure.

In 33 catheterizations in which a smear was obtained of inner catheter urine there were nine positive smears. Urine cultures and catheter-tip cultures (outer and inner) in the same nine catheterizations were positive for the same micro-organisms as the smears. On the other hand, there were five catheterizations in which the outer catheter urine smear was positive and the corresponding urine culture or urine culture and catheter-tip culture were negative. We can only speculate on the possible reasons for this. In most cases the micro-organisms seen on smear were rare. Failure to grow in the tryptose phosphate broth may have been due to a difference of acidity or to some inhibiting substance in the urine. It is also difficult to say whether these positive smears represent prior urinary infection or contamination, although in at least two instances it seems probable that the micro-organism was a contaminant. This is contrary to the experience of Sanford and co-workers,[5] who did not find any negative cultures associated with positive smears.

The aim of the present study has been the discovery of a means of preventing or at least lessening the risk of contamination in obtaining a bladder urine culture. Other investigators[4] have sought means of recognizing contamination by doing quantitative bacterial cultures, the probability being high that one is dealing with a contaminant where the bacterial count is low.

Summary

In a new method of obtaining a bladder urine specimen for culture from female patients, bladder urine is obtained through a small rubber catheter inserted into the bladder through a larger catheter inserted only into the urethra and not into the bladder. The purpose of the latter is to protect the inner catheter from contamination from micro-organisms present in the urethra. In the present investigation a bladder urine specimen was also obtained through the outer catheter by advancing it into the bladder after removal of the inner catheter, a procedure which is essentially the same as the standard technique for obtaining a bladder urine culture specimen.

Cultures were made of the catheter tips, and cultures and direct smears were made of the urine specimens. There were 45 catheterizations in 38 female patients. The outer catheter urine cultures were positive in 52%; the inner catheter urine cultures were positive in 32%. The outer catheter-tip culture was positive in 89% of the catheterizations and the inner catheter-tip culture in 52%. The direct smears of the outer catheter urine were positive in 54%; those of the inner catheter urine were positive in 27%. Where both outer and inner catheter specimens were obtained in the same catheterization there was a micro-organism present in the outer catheter specimen not present in the inner in 27% of the urine cultures and in 59% of the catheter-tip cultures. The reverse situation was obtained in 2.5% of the urine cultures and in 20% of the catheter-tip cultures.

Since there is an appreciably lower frequency of positive cultures in the inner catheter series and since the procedure described is not difficult to perform, it is felt that it may have some practical application.

720 N. Michigan Ave. (11) (Dr. Rhoads).

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FEBRILE TRANSFUSION REACTIONS CAUSED BY SENSITIVITY TO DONOR LEUKOCYTES AND PLATELETS

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The hypothesis that some otherwise unexplained febrile reactions to blood transfusions may be caused by isoimmunization of patients against the donors' leukocytes was tested in 10 patients who needed transfusions. Five patients (group A) had previously had from 20 to 85 transfusions, had histories of repeated transfusion reactions, and had demonstrable antibodies against the specific normal leukocytes administered during this study. The other five patients (group B) had had only seven or less previous transfusions, with no histories of transfusion reactions. Group A did not experience adverse effects when the blood used for transfusion was so prepared, by centrifuging, as to remove as much as possible of the buffy layer, but all reacted with fever, typical symptoms, and characteristic laboratory findings to subsequent transfusion of the buffy coat which had been so removed. Group B did not react adversely to either fraction of the donors' blood. Immunologic evidence suggested that it was the leukocytes rather than the platelets in the buffy layer that caused the reactions. Techniques for removing the buffy coat when blood is prepared for transfusion offer a means of preventing the dangerous reactions that occur when patients, after multiple transfusions, become isoimmunized to donor leukocytes.

Unexplained febrile reactions to transfused blood are frequent, accompanying more than 1% of all transfusions. They are distressing and sometimes dangerous. They occur especially in patients who receive multiple transfusions and have been considered of "nonspecific" origin because of inability to demonstrate contamination of the blood, presence of pyrogens, red blood cell incompatibility, or sensitivity to the donor's plasma.

In a systematic study of the occurrence of antileukocyte agglutinins, we and others [1] have been struck by the presence of strong leukoagglutinins in the serums of most patients who had received multiple transfusions and who gave a history of repeated severe febrile transfusion reactions. The white blood cell agglutinins were typical isoantibodies, showing no activity whatsoever against the patient's own leukocytes but clumping a wide range of normal donor leukocytes. In addition, several patients when first seen were able to receive transfusions without any symptoms. No leukoagglutinins were demonstrable in their serums at that time. Subsequently, after they began to have distressing febrile reactions to transfusions, they were found to have developed leukoagglutinins.

The present study was undertaken to explore the possibility that the leukoagglutinins were causally related to the transfusion reactions experienced by these patients.

Methods

To study more definitively the relationship of transfusion reactions to leukoagglutinins, five reaction-prone patients and five control patients were transfused with fractionated blood, one part poor in white blood cells and platelets, the other rich in these elements. After all transfusions the recipient's temperature, other vital signs, white blood cell count with differential, and sometimes platelet count were followed at frequent intervals for at least six hours. One of us stayed at the subject's bedside throughout the reaction to observe symptoms and signs.

Patients.—All subjects were patients under the care of the division of hematology on the wards of the Barnes Hospital group or in the outpatient departments of the Washington University Clinics. Pertinent descriptive data are summarized in table 1.

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Read in part before the American Society for Clinical Investigation, Atlantic City, N. J., May 6, 1957.

Five patients (cases 1 to 5) gave a history of repeated severe febrile transfusion reactions. The white blood cell agglutinins in all five of these patients were isoantibodies, i. e., they were completely inactive against the patient's own leukocytes. It is of interest that two of these five patients had no agglutinins against donor platelets and two others had only very weak agglutinins. An indirect Coombs cross-match was performed prior to each transfusion. One patient (case 5) could not be satisfactorily cross-matched with any donor red blood cells. It is interesting that fraction 1 (see below) caused this patient no detectable reaction, and the chromium-tagged red blood cells with which he was transfused were not rapidly destroyed. The

control patients (cases 6 to 10) were chosen because they were comparably anemic, gave no history of transfusion reactions, had no leukoagglutinin demonstrable in their serums, and were not taking antipyretic, antihistaminic, or steroid medicaments. All patients required transfusion therapy at the time they were studied.

Separation of Donor Blood into Fractions 1 and 2.—The process of separating donor blood into fractions consisted of six steps.

Step 1: From 500 to 550 ml. of blood was drawn from a normal donor into plastic bag A (Ethicon) (fig. 1.), containing 50 ml. of 1.5% disodium ethylene diamine tetra-acetic acid (EDTA) anticoagulant solution. The hematocrit, white blood cell

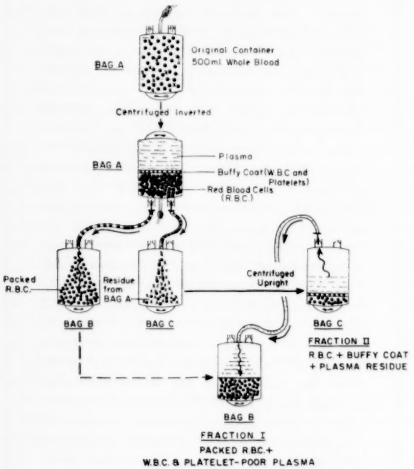

Fig. 1.—Method for separating blood into fractions 1 and 2.

count, and platelet count of the collected donor blood were determined from either (*a*) a sample of the bag's contents obtained after thorough mixing or (*b*) a sample collected from the donor at the conclusion of donation, with the results corrected by multiplying by 500/550 to allow for dilution by the anticoagulant solution. Siliconed tubes were used for all samples.

Step 2: Bag A was centrifuged in the inverted position at 1,800 rpm for 40 minutes in a refrigerated centrifuge of 26-cm. radius (from the center to the base of the cup in the horizontal position). Bag A was removed from the centrifuge cup with great care to avoid disturbing the white blood cells and platelets (buffy coat) concentrated at the plasma–red blood cell interphase.

Step 3: A dry bag, B, was connected to bag A and then placed on a balance. From 150 to 180 Gm. of packed cells was allowed to flow into bag B. The connecting tubing was clamped just distal to the outlet from bag A.

Step 4: The contents of bag A were thoroughly mixed and allowed to drain into bag C (of 400-ml. capacity). Bag C was centrifuged in the upright position but otherwise exactly as described for bag A.

Step 5: The coupler from bag B was then disengaged from bag A and inserted into one of the outlets of bag C. Approximately 200 ml. of the supernatant plasma was expressed into bag B, and the connecting tubing was clamped just proximal to the coupler. This red blood cell–plasma mixture constituted fraction 1 and contained approximately 75% of the red blood cells, 60% of the plasma, and less than 10% of the white blood cells and platelets originally bled from the donor (see table 2). The connecting tubing was tied close to bag B and cut distal to the knot. The residue remaining in bag C constituted fraction 2 and contained approximately 25% of the red blood cells, 60% of the plasma, and over 90% of the white blood cells and platelets from the original donor blood.

Step 6: The connecting tubing attached to bag C was cleared of plasma by stripping through a tightly closed Kelly clamp protected by rubber guards. The contents of bag C were then thoroughly mixed by vigorous kneading of the limp bag against the hard table top surface. The resuspension required approximately five minutes. The bag was inverted and approximately 5 ml. of the contents was allowed to drain from the tubing (discard), and then a 3-ml. sample was collected in a siliconed tube for determination of hematocrit, white blood cell count, and platelet count. The tubing was then tied close to the coupler and the bag immediately placed in the blood bank storage refrigerator (at 4 C), where it remained until its administration on the following day.

Fraction 1 was thoroughly mixed and a 3-to-5-ml. sample collected from the distal end of the plastic transfusion administration set. The transfusion of fraction 1 was begun immediately thereafter.

Cultures.—No cultures were made of material from fraction 1, which was administered to the recipient within four hours of drawing the blood from the donor. Immediately prior to administration of fraction 2 (which had been stored at 4 C for 16 to 18 hours), a sample of the well-mixed contents was cultured on a blood agar plate and in three tubes of thioglycollate broth. Cultures were incubated at 37 C. All cultures showed no growth and were discarded after 48 hours (blood agar) and 72 hours (thioglycollate broth).

Administration of Transfusions.—In each study, the rate of administration was the same for both fraction 1 and fraction 2 and was approximately

15 ml. per minute. Thus, the time required for administration of fraction 1 ranged from 15 to 30 minutes and for fraction 2 from 5 to 15 minutes.

Hematologic Studies.—White blood cell counts and hematocrit were determined by standard methods as described by Wintrobe.[2] Platelets were counted by the direct method,[3] with use of phase-contrast microscopy. Platelet agglutinins were determined by the method of Harrington.[4] Leuko-agglutinins were determined by a method developed by one of us (T. E. B.), modified from the procedure described by Dausset and co-workers.[5] Fifteen milliliters of blood from a normal donor was taken into a siliconed tube containing 0.4 ml. of 5% EDTA anticoagulant. The blood was sedimented for about two hours at refrigerator temperature. The supernatant plasma and buffy coat were removed with a capillary pipette and centrifuged at 200 rpm for 15 minutes. The small white blood cell button at the bottom of the tube was suspended in about 0.75 ml. of 20% bovine albumin to make the white blood cell suspension. About 0.05 ml. of cell suspension was incubated with about 0.10 ml. of test serum for 90 minutes at 37 C. The tests were read under 100× magnification, though significant agglutination was usually readily visible grossly. Testing was completed within eight hours of drawing the blood for the white blood cell preparation. EDTA, in a concentration of 0.4 ml. of 5% EDTA to 8 ml. of serum, was added to all test serums to prevent clotting (and concomitant nonspecific agglutination) of the white blood cell preparation.

Results

Characteristics of Fractions 1 and 2.—Blood cell counts and hematocrit were determined in an aliquot of the original donor blood and of each fraction to demonstrate that there had been no significant loss of white blood cells or platelets and that an appropriate fractionation had been accomplished. The characteristics of the collected donor bloods were not remarkable; hematocrits ranged from 39% to 47%, white blood cell counts from 6,500 to 8,800 per cubic millimeter, and platelet counts from 180,000 to 303,000 per cubic millimeter.

The characteristics of fractions 1 and 2 are summarized in table 2. It will be noted that the sum of the volume of fraction 1 plus the volume of fraction 2 does not always equal 550-600 ml. A total of approximately 20 ml. was removed in sampling during the various stages of preparation. In addition, in order to intensify the contrast between fractions 1 and 2, on several occasions (transfusions to patients in cases 1, 2, and 3) up to 40 ml. of packed cells was discarded at the conclusion of step 3. In three instances (transfusions to patients in cases 1, 4, and 5), in order to diminish the total volume of the fractions, up to 150 ml. of plasma was discarded during step 6. It is evident that there

TABLE 1.—*Data on Five Patients with History of Transfusion Reaction and Five Controls*

Case No.*	Age, Yr.	Sex	Diagnosis	Previous Transfusions, No.	Demonstrable Antibodies Against Donor†	
					WBC‡	Platelets
1	21	M	Hypoplastic anemia	75	1:128	–
2	52	M	Acute monocytic leukemia	31	1:16	+++
3	30	F	Anemia and thrombocytopenia	85	1:16	Weak
4	32	M	Immunized normal subject	20	1:4	Weak
5	75	M	Primary red blood cell aplasia	56	1:512	–
6	45	F	Iron deficiency anemia	7	–	–
7	20	F	Blood loss anemia	2	–	–
8	66	F	Chronic lymphocytic leukemia	2	–	–
9	72	F	Thymoma; red blood cell aplasia	7	–	–
10	76	M	Chronic lymphocytic leukemia	3	–	–

* Patients in cases 1-5 had history of transfusion reaction; those in cases 6-10 were controls.
† Patient in case 5 was only one with demonstrable antibodies against donor red blood cells.
‡ Antibody titers of subjects' leukoagglutinin against specific normal white blood cells administered during study.

TABLE 2.—*Characteristics of Fractions 1 and 2 of Donor Blood*

Case No.	Fraction 1						Fraction 2					
	Total Volume, Ml.	Hemato-crit, %	Volume RBC, Ml.	Volume Plasma, Ml.	WBC $\times 10^3$/ Cu. Mm.	Platelets $\times 10^3$/ Cu. Mm.	Total Volume, Ml.	Hemato-crit, %	Volume RBC, Ml.	Volume Plasma, Ml.	WBC $\times 10^3$/ Cu. Mm.	Platelets $\times 10^3$/ Cu. Mm.
1	228	74.0	169	69	0.05	3.5	85	44.0	37	48	59.40	1,220
2	310	43.5	135	175	0.20	6.5	145	28.2	41	104	16.35	890
3	395	41.0	162	233	1.30	7.5	165	23.0	38	127	15.90	700
4	300	64.0	192	108	1.20	8.8	146	41.0	60	86	28.50	870
5	280	60.5	170	110	1.20	10.0	238	43.0	103	135	22.20	663
6	400	53.0	212	188	0.75	29.0	180	32.0	58	122	25.00	1,035
7	420	44.0	185	235	1.65	12.5	148	36.5	54	94	21.90	590
8	343	50.0	172	171	1.30	21.0	142	44.0	62	80	19.95	705
9	421	42.0	177	244	0.56	8.0	163	42.0	68	95	30.90	795
10	414	49.0	203	211	0.50	11.0	162	40.0	65	97	23.90	545

was considerable variation among the different donor bloods in the efficiency of concentration of the buffy coat elements into fraction 2. The reasons for these variations were not always apparent. Preliminary studies showed that, if more than 75% of the packed red blood cells were withdrawn after centrifugation under the conditions described in the section on methods, the white blood cell count of fraction 1 rose sharply. This indicated that, although the lower margin of the buffy coat appeared to be discretely defined, a significant gradient of white blood cells existed in the upper quarter of the packed red blood cell mass. Although every effort was made to standardize the various processing procedures, minor differences in technique undoubtedly influenced the effectiveness of the buffy coat separation. In addition, a strong impression was gained that donor differences played a significant role, some donor bloods apparently lending themselves to buffy coat separation more readily than others. More than 90% of the donor blood's white cells were present in fraction 2 in 7 out of

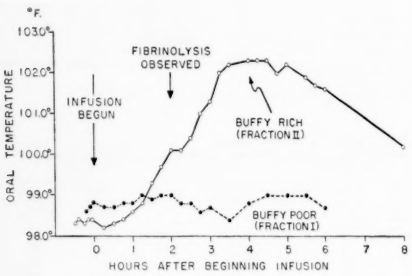

Fig. 2.—Reaction of patient in case 1 to infusion of fractions 1 and 2.

the 10 studies (cases 1, 2, 4, 5, 6, 9, and 10). In the remaining three studies (cases 3, 7, and 8) fraction 2 contained 80 to 86% of the white blood cells. Effective separation of platelets was more consistently accomplished, with more than 95% of the original platelets present in fraction 2 in every instance.

Response to Transfusions.—Figures 2 through 6 show the oral temperature curves of the patients in cases 1 through 5, respectively, after they had received fractionated blood. None of these subjects experienced symptoms of any kind after infusion of fraction 1. In none was there a rise above the usual daily temperature, nor was there any significant change in white blood cell or differential counts. After administration of fraction 2, however, all five patients had marked febrile and symptomatic responses, the important features of which will be summarized briefly for each patient. All patients commented that the reactions were exactly like their usual transfusion reactions except that some of the experimental reactions were milder than those to which the patient was accustomed.

Case 1 (fig. 2).—Fifty-nine minutes after the infusion of fraction 2 was begun, this man experienced a feeling of chilliness which did not, however, progress to frank rigor

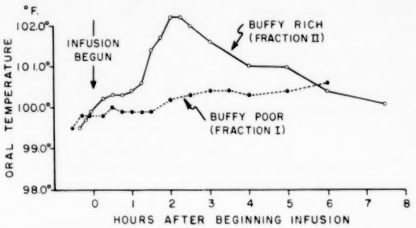

Fig. 3.—Reaction of patient in case 2 to infusion of fractions 1 and 2.

(in contrast to the other four patients). His oral temperature reached a peak of 102.3 F (39 C), and he experienced marked apathy and prostration persisting for approximately five hours. Note also that blood drawn from the subject two hours after beginning the transfusion showed complete spontaneous fibrinolysis (fig. 2).

Case 2 (fig. 3).—Seventy-eight minutes after the infusion of fraction 2 was begun, this man experienced a shaking chill lasting for 16 minutes. The chill was followed by a rise of oral temperature to 102.2 F (39 C). Minor symptoms of weakness and apathy persisted for approximately 45 minutes.

Case 3 (fig. 4).—Sixty-two minutes after the infusion of fraction 2 was begun, this woman experienced a shaking chill lasting for 21 minutes, followed by headache, backache, moderate weakness, and exhaustion continuing during the ensuing one to two hours. It is interesting that, although this patient had a rise in oral temperature of 2.4 F (1.3 C) above her baseline level, the peak was only to 100.3 F (38 C). Two factors may have accounted for the less marked temperature elevation observed in this patient. From table 2 it can be seen that much the poorest separation of buffy coat

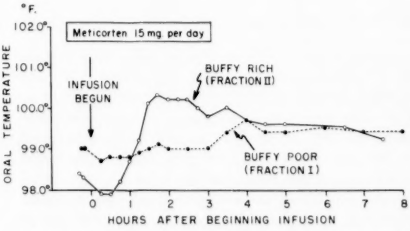

Fig. 4.—Reaction of patient in case 3 to infusion of fractions 1 and 2.

between the two fractions was accomplished in this instance. In addition, the patient was receiving 15 mg. of prednisone (Meticorten) daily at the time the study was performed (in contrast to the other four patients and to the five control subjects). We have observed in other experiments, not in-

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cluded in this report, that prednisone is probably able to diminish the febrile response in transfusion reactions caused by sensitivity to buffy coat.

Case 4 (fig. 5).—Fifty-five minutes after the infusion of fraction 2 was begun, this man experienced a shaking chill lasting 22 minutes, followed by a rise in oral temperature to

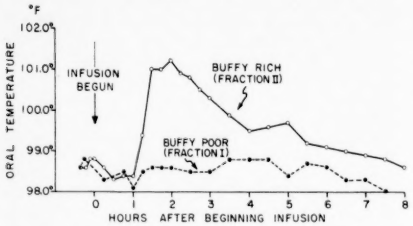

Fig. 5.—Reaction of patient in case 4 to infusion of fractions 1 and 2.

101.2 F (38.5 C). Headache, irritability, and marked lassitude persisted for five hours. Incidentally, this subject is a healthy laboratory worker who was deliberately isoimmunized to white blood cells to permit more detailed study of the relationship of leukoagglutinins to transfusion reactions.

Case 5 (fig. 6).—Fifty-two minutes after the infusion of fraction 2 was begun, this seriously ill 75-year-old man experienced a severe shaking chill lasting 52 minutes, a rise in oral temperature to 102.4 F (39.1 C), cyanosis, gallop rhythm, markedly impaired mentation with disorientation and amnesia, and a profound prostration lasting about nine hours. This life-threatening episode represented a typical febrile transfusion reaction for the patient.

Hematological Observations.—The patient in case 2, who had acute monocytic leukemia with a white blood cell count of 132,000 per cubic millimeter consisting of more than 90% blast cells, was the only patient who did not show a marked fall in

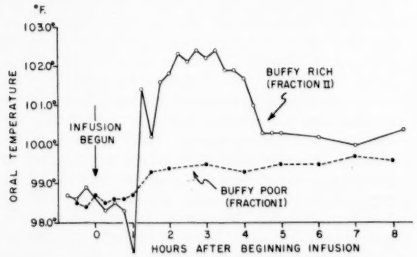

Fig. 6.—Reaction of patient in case 5 to infusion of fractions 1 and 2.

neutrophil count within 15 minutes of the beginning of the infusion of fraction 2. All five patients later showed a marked rise in neutrophil leukocytes above control levels, maximum values being reached within two to five hours after transfusion.

The occurrence of fibrinolysis in one patient (case 2) has already been mentioned; we have observed this phenomenon in at least one other similar study, not included in the present series.

Pattern of the Reaction.—There was a remarkable consistency in the pattern of the reactions which followed the transfusion of fraction 2 to this group of patients. These always consisted of (1) an immediate reaction, (2) a latent period, and (3) a delayed reaction. The characteristics may be summarized as follows: The immediate reaction was transient, with onset within five minutes of the beginning of the transfusion, and consisted of flush, palpitation, tachycardia, cough, a "thick choking" feeling in the chest, and neutropenia. The latent period occupied the interval from 15 to 60 minutes after the beginning of the transfusion. During this time, the patients all felt entirely well. The delayed

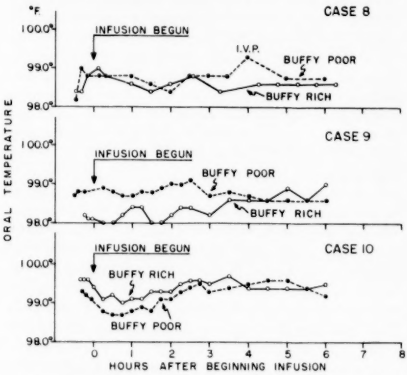

Fig. 7.—Reactions of three control patients (cases 8, 9, and 10) to infusion of fractions 1 and 2.

reaction had its onset approximately one hour after the beginning of the transfusion. This phase was heralded by a rise in the diastolic blood pressure and the onset of headache and chilliness with progression to frank rigor, followed by a rapid rise in temperature. Apathy, irritability, probably impaired mentation, and prostration persisted for several hours thereafter. A neutrophil leukocytosis with a marked shift to the left reached its peak two to five hours after the beginning of the infusion.

Control Subjects.—Figure 7 shows the temperature curves of three of the five control patients after they received fractionated blood. The other two control subjects showed entirely similar responses. There was no rise in temperature, and no control patient had symptoms, physical signs, leukopenia, or leukocytosis after receiving either fraction 1 or fraction 2.

Comment

These studies strongly suggest that isosensitization to elements of the buffy coat is causally related to the recurring febrile transfusion reactions experienced by some patients who have received multiple transfusions. Human donors' leukocytes appear to be effective antigens, and it is likely that useful information will evolve from the application of modern immunological techniques to the study of normal and diseased white blood cells. We believe that sensitivity to white blood cells is more important than sensitivity to platelets as a cause of febrile reactions, because the reactions correlate consistently with the presence of leukoagglutinins in the recipient's serum but only erratically with the presence of platelet agglutinins.

Dameshek and Neber [6] have shown that sensitization to some constituent of donor plasma may occasionally provoke febrile reactions. In two of their patients the causal relationship of infusion of the donor's plasma to the patient's reaction was unquestionably established when the infusion of as little as 9 to 20 ml. of centrifuged plasma (presumably free of platelets and white blood cells) was followed by chills and fever. In several other patients who had received multiple transfusions, provocation of reactions by the infusion of centrifuged plasma was not attempted, but sensitivity to plasma was presumed to be the cause of this when it was shown that the administration of thoroughly washed red blood cells was not accompanied by the usual chills and fever. It may be wondered whether certain of these latter patients were actually isosensitized to the buffy coat, since, in our experience, the process of washing red blood cells may result in the removal of more than 80% of the buffy coat in addition to over 98% of the plasma.

The complete absence of fever and symptoms in the five control subjects in the present study suggests that the febrile reactions observed in the first five patients were not caused by a nonspecific febrile effect of stored white blood cell concentrates nor by contamination of fraction 2 with bacterial pyrogens or with cold-growing bacteria which were not detected in the cultures incubated at 37 C.

To establish that the processing and storage of white blood cells are not essential to the production of febrile reactions in sensitized patients, one patient (case 4) was transfused by siliconed syringe technique with blood containing leukocytes to which he was sensitive. These white blood cells were out of the donor's circulation for less than one minute before being infused into the recipient. Their injection resulted in a typical severe reaction, with shaking chills and fever.

The patients in cases 1 and 3, who were accustomed to receive a pint of blood on two successive days about once monthly, reported that they almost invariably had a much less severe reaction to the second pint than to the first. This observation was somewhat unexpected, because their leukoagglutinins were present in great excess of the number of transfused white blood cells and the titers of the leukoagglutinins were not significantly decreased by the initial transfusion. The tendency to have a less severe reaction on the day following a severe transfusion reaction is suggestive of the phenomenon of tolerance seen with successive injections of bacterial pyrogen. Both phenomena develop rapidly and are of short duration. Tolerance to bacterial pyrogens is unrelated to the development or the saturation of antibodies. The composition of fractions 1 and 2 and the order in which they were administered in the present experiments were designed with the possibility of tolerance in mind. It is apparent that the absence of reactions following the administration of fraction 1 and their regular occurrence following administration of fraction 2 constitute strong evidence for a primary causative role for the elements of the buffy coat, as opposed to the red blood cells and plasma.

The febrile transfusion reactions exhibited by patients with buffy coat sensitivity show many similarities to the reaction seen in patients following injection of bacterial pyrogen. Thus, there is the possibility that tolerance develops to repeated leukocyte-leukoagglutinin reactions just as it does to repeated injections of bacterial pyrogen. With both reactions, there is a period of latency of approximately one hour during which the patient has a sense of complete well-being before the onset of chills and fever. The symptoms and signs in both reactions are alike. Fibrinolysis may occur in both syndromes. Changes in the white blood cell count follow an identical pattern in both (immediate transient neutropenia followed later by leukocytosis with a shift to the left). Finally, both syndromes vary sharply in severity with the amount (dose) of provocative substance (white blood cells or pyrogen) administered. Stetson [7] has pointed out that the effect of intravenous injection of bacterial pyrogen in normal rabbits is very similar to the effect of intravenous administration of tuberculin in specifically hypersensitive rabbits. He advances the hypothesis that some basic mechanism may be common to both reactions. Jandl [8] has recently pointed out the similarity between reactions to bacterial pyrogen and the reactions which follow immune hemolysis in man. The present study of febrile transfusion reactions in patients with buffy coat sensitivity would seem to be further evidence of a close relationship between the basic mechanisms underlying reactions to bacterial pyrogens and reactions associated with various hypersensitivity states.

Some of the symptoms and signs of the reactions secondary to buffy coat sensitivity can probably be suppressed by the use of such drugs as antipyretics, antihistaminics, or adrenal steroids. However, since

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it is known that pyrogens (and by analogy leukocytes given to a sensitive recipient) are harmful, that they produce diffuse capillary and endothelial damage, impair function of vital organs, and cause necrosis in tumors,[9] it is likely that simple suppression of symptoms may be unwise. The reactions can be prevented in a more direct way by removing leukocytes and platelets from the blood to be transfused. Buffy coat–poor blood can be prepared in the manner which has been described for these investigations. An alternate method, in which the red blood cells are sedimented in dextran (mean molecular weight approximately 140,000), is currently undergoing clinical trial by one of us (H. C.). This procedure, which does not require centrifugation, has the advantages of technical simplicity, effective removal of over 95% of the buffy coat, and economy of donor red blood cells, more than 98% being available for transfusion in contrast to 70-75% by the method of centrifugation. Buffy coat–poor transfusions are being successfully employed in the management of several seriously ill reaction-prone patients.

Summary and Conclusions

Donor leukocytes are effective antigens. Patients who receive multiple blood transfusions may become isoimmunized to the leukocytes and probably also the platelets in the transfused blood. Isoantibodies against white blood cells and probably against platelets are a common cause of repeated febrile transfusion reactions. The reactions show a striking resemblance to reactions seen in patients after the injection of bacterial pyrogen. The reactions, which can be severe and occasionally threatening to life, can be prevented by removal of the buffy coat prior to administration of the blood.

600 S. Kingshighway (10) (Dr. Chaplin).

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We are indebted to Dr. Wilbur Mattison for performing the platelet agglutinin tests included in this report.

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Management of Bleeding Diseases.—In general, whole blood is used to correct the anemia of acute or chronic blood loss in the bleeding diseases and whole blood or plasma may be used to prevent shock. Plasma is also used to replace needed coagulation constituents. Fresh whole blood or plasma, fresh frozen plasma, or fresh lyophilized plasma is desirable in the treatment of antihemophilic globulin (AHG) deficiency, labile factor deficiency and fibrinolytic states. Platelet-rich plasma or fresh plasma collected in silicone-coated or plastic containers, or direct transfusion, may be helpful in patients with thrombocytopenia. Bank blood, or plasma (not more than 30 days old), is indicated in plasma thromboplastin component (PTC) and plasma thromboplastin antecedent (PTA) deficiency, stable factor deficiency, hypoprothrombinemia, afibrinogenemia and fibrinogenopenia. Cohn Fraction I has been employed successfully in AHG deficiency and afibrinogenemia (or fibrinogenopenia). Vitamin K has proved to be effective in prothrombin deficiency due to insufficient dietary intake or absorption of vitamin K. Vitamin K_1 and K_3 oxide are also extremely valuable in the treatment of the hypoprothrombinemia of Dicumarol administration. ACTH, cortisone and related compounds have considerable importance in the management of the acute phase of idiopathic and symptomatic thrombocytopenic purpuras, some of the non-thrombocytopenic purpuras and excessive fibrinolysis. Splenectomy may be indicated in idiopathic thrombocytopenic purpura resistant to steroid therapy. Bed rest with local pressure, topical application of coagulants, or other local hemostatic measures should always be used, where applicable, to help in controlling active bleeding of the affected part or parts.—A. J. Johnson, M.D., The Management of Acute Episodes in Patients with Bleeding Diseases, *The Medical Clinics of North America*, May, 1957.

CLINICAL NOTES

A PORTABLE CHAIR-SCALE FOR HOSPITAL USE

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A patient's weight record is an important source of clinical information. Like the pulse and temperature curve, the appraisal of a weight record can be of tremendous diagnostic aid. In the management of congestive heart failure, kidney and endocrine disturbances, electrolytic and nutritional problems, and many postoperative states, a daily weight record is often invaluable.

Fig. 1.—Portable chair-scale.

For a variety of reasons, unfortunately, daily fluctuations in body weight are too often neglected or reported haphazardly. In our experience, the most important reason daily weight records are not available in an average hospital ward is the absence of a convenient, practical method for weighing patients. In the average busy hospital, the technique for weighing patients is not sufficiently organized nor is its importance emphasized. As a result, the physician's request to weigh a patient daily tends to become a chore and is relegated to the last order of business. Actually, the procedure for weighing patients should be less time consuming than taking temperature readings. Various complicated scales have been designed to weigh patients confined to bed.[1] Most of these arrangements, however, are expensive and unwieldly and consequently not available to the average hospital. The household bathroom scale is too unreliable and generally not practical for the patient in a hospital bed.

It is our purpose to describe an inexpensive, portable scale for hospital use (fig. 1). A seriously ill patient is usually able to sit but too weak to stand. This fact initiated the development of the chair-scale. An upright beam scale (fig. 2, *B*) is mounted on a platform (fig. 2, *H*) constructed with ¾-in. plywood, measuring approximately 30 by 20 in. This platform is made mobile by the insertion of a sturdy ball-bearing rubber caster at each corner (fig. 2, *E*). Another plywood base, measuring 23 by 20 in.

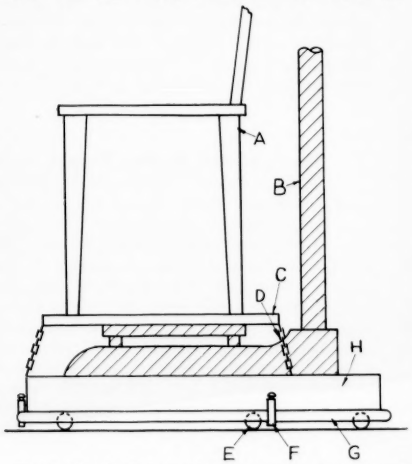

Fig. 2.—Sketch of chair-scale—side view. *A*, chair; *B*, scale; *C*, platform mounted on scale; *D*, chain from platform to base; *E*, rubber caster; *F*, door stop; *G*, sideboard attached to platform base, *H*, on which scale rests.

From the Department of Medicine, Staten Island Hospital.

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(fig. 2, *C*) is bolted to the platform of the scale. Excess motion of the scale platform base is restricted by chains at each side (fig. 2, *D*). To prevent rolling while the chair-scale is in use, friction door brakes or stops (fig. 2, *F*) are mounted on sideboards (fig. 2, *G*). The brakes are conveniently manipulated by foot. The balance-control screw of the scale should be adjusted to compensate for the added weight of the chair and platform. Aside from the chair and the scale, this entire unit can be assembled in a carpenter shop at a cost of less than $5.

The chair-scale is comfortable for the patient and is remarkably simple to operate. It is rolled to the bedside and the foot stops are applied. The patient is then assisted to, or lifted into, the armchair, where he sits comfortably for a few moments while the weight is recorded. This procedure is carried out routinely on the ward every morning at approximately the same time. In an open ward of 20 patients, less than 30 minutes are consumed by this method. This technique should be applicable to most hospital patients except those confined to the supine or prone position. For over two years this scale arrangement has been an integral part of the ward routine of this hospital.

Summary

An inexpensive chair-scale has been designed for weighing the majority of hospital patients. This scale is portable, comfortable, and easy to manipulate. It is important to establish an organized routine for weighing hospital patients.

100 Central Ave. (1) (Dr. Silverman).

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SIGMOIDOUTERINE FISTULA COMPLICATING DIVERTICULITIS

REPORT OF A CASE

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and
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In a recent case report and review of the literature, Franco and Clough [1] noted reports, including their own, of 75 cases of enterouterine fistula. These cases occurred following (1) carcinoma of either the intestine or uterus with subsequent invasion of the other structure and communication of the lumina, (2) rupture of the uterus (either spontaneous or produced during labor), or (3) inflammatory disease (such as pathological puerperium and appendicular abscess) causing peritonitis. Under this last heading, diverticulitis with abscess formation may be included.

Only two cases of sigmoidouterine fistula complicating diverticulitis have been reported prior to the time of this writing, one by Noecker,[2] in 1929, and another by Johnston and Stubbs,[3] in 1955. The advised treatment consists of preliminary preparation of the patient with antibiotics, sterilization of the intestine, diet, and transfusions. Johnston and Stubbs felt that, in the absence of infection and obstruction, primary resection of the colon should be performed. Franco and Clough felt that, in the absence of considerable reaction and inflammation or an opening in the intestine too large to be closed effectively, the involved viscera could be separated and the openings sutured.

Chief Resident in Surgery (Dr. Smalley); Attending Surgeon (Dr. LoRusso); and Chief, Surgical Service (Dr. O'Brien), St. Vincent's Hospital.

A 76-year-old female was admitted to the surgical service of St. Vincent's Hospital on July 23, 1956, complaining of constant discharge of liquid feces per vaginam for the previous seven and one-half weeks. The patient stated that while she was lying quietly in bed on June 1, 1956, she heard a peculiar "snapping" noise that seemed to emanate from her pelvis; she passed a small amount of mucus vaginally, and, within a few minutes, the discharge of liquid feces began. The patient had been seen in medical clinic, where discharge of feces from the cervical os was observed.

The patient had been followed in the medical and diabetic clinic for a number of years. Her medical history included diabetes mellitus, which had been diagnosed 12 years previously; at the time of admission she was taking 35 units of isophane insulin daily. Due to hypertensive and arteriosclerotic heart disease, the patient had required digitalis daily for two years. A substernal goiter had been present for 18 years, apparently without evidence of recent thyroid activity. The patient had three children; the last menstrual period had been in 1936; no vaginal bleeding had occurred since that time. No prior surgical procedure had been performed. The patient denied all symptoms referable to the gastrointestinal and urinary tracts. She had had no loss of weight; she had had no pain at any time.

Physical examination on admission disclosed a thin, elderly, cooperative female, who appeared chronically ill. There were funduscopic changes consistent with diabetes and arteriosclerosis; examination of the head and neck was otherwise not remarkable. The chest was symmetrical; the lungs were clear and resonant throughout. The heart tones were of good quality, rhythm was regular, and a blowing systolic murmur was heard over the entire precordium. The abdomen was obese and soft; the liver edge was palpable 4 cm. below the right costal margin.

No other viscera or masses were palpable, and no tenderness was elicited. Pelvic examination disclosed brown fecal material in the vagina and mild erosion of the cervix. Rectal examination disclosed no pathology.

Careful examination of the vagina, after the feces had been cleaned out, combined with proctoscopic examination and the use of methylene blue, failed to demonstrate any fistulous tract between the rectum and vagina. X-ray, after a barium enema on July 27, showed sigmoid diverticulitis, and in an oblique view (fig. 1) the presence of a tract leading to a nearby cavity was demonstrated. A hysterosalpingogram made on July 30 confirmed the impression that the nearby cavity was the uterine cavity; chloriodized oil (Iodochlorol) injected into the uterus under the fluoroscope appeared in the sigmoid within 10 seconds; x-ray (fig. 2) again showed the sigmoid diverticulitis, fistulous tract, and uterine cavity.

After a medical staff consultation, the patient's cardiac and diabetic status was improved, and she was prepared for operation. Laparotomy was done on Aug. 2. A fistulous tract 5 cm. in length and 2 cm. in diameter was found extending from the antimesenteric border of the midsigmoid to the fundus of the uterus and entering the uterine fundus at a point 1 cm. superior to the entrance of the right fallopian tube. Adhesions surrounding the fistula involved the sigmoid, the uterus, and the bladder. No acute inflammatory process was present. Further examination of the abdomen revealed the absence of gross pathology in the liver, gallbladder, stomach, small intestine, omentum, mesentery, kidneys, and colon as far as the sigmoid. There were no palpable iliac or aortic lymph nodes. Multiple small sigmoid diverticula were noted.

Because of the patient's age, heart disease, diabetes, and substernal goiter and her expressed fear of a colostomy, and in view of the absence of acute inflammation and the small (2-cm.) diameter of the opening of the tract in the intestine, it was decided to attempt resection of the fistulous tract and closure of the intestine in accord with the opinion of Franco and Clough. Accordingly, the adhesions between bladder and sigmoid were separated, and, upon careful dissection of the sigmoid-uterine adhesions, the fistula was entirely exposed. A negligible amount of bleeding was encountered. The fistulous tract, including a small amount of necrotic tissue at each end, was removed. The opening in the sigmoid was closed transversely in two layers. A probe was passed through the uterine opening and the cervical os and was immediately recovered in the vagina. The opening in the uterus was closed with chromic absorbable surgical sutures.

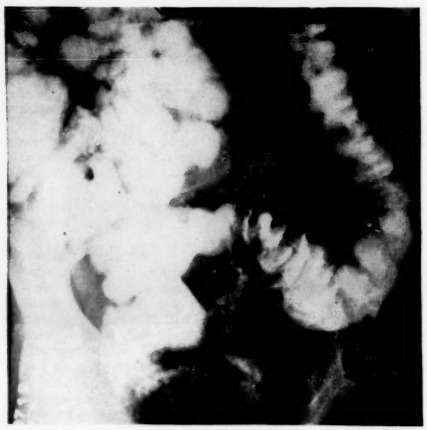

Fig. 1.—Roentgenogram showing evidence of sigmoid diverticulitis after barium enema had been given.

Postoperatively, the patient's course was remarkably smooth. She began to have normal stools on the third postoperative day. On the eighth postoperative day, she developed a mild cystitis. Complete urologic studies failed to disclose evidence of any other pathology, and the cystitis cleared within a few days.

Fig. 2.—Roentgenogram showing sigmoid diverticulitis, fistulous tract, and uterine cavity.

After the medical consultant had placed her on an outpatient regimen consisting of diet, insulin, and digitalis, the patient was discharged three weeks after operation.

The patient was subsequently seen at periodic intervals. She has had no symptoms or signs of any recurrence of the disease which brought her into the hospital. Physical examination, including pelvic and rectal examinations, has revealed no evidence of pathology. The mucous membrane of the sigmoid and the cervix are normal in appearance. The patient has been doing her normal housework and has had no symptoms referable to the gastrointestinal or urinary tracts. She was last seen one year after operation.

Summary

A case of sigmoidouterine fistula complicating diverticulitis, complicated by the presence of diabetes, was successfully treated by means of excision of the fistulous tract and closure of the openings in the sigmoid and uterus. Reports of two cases of sigmoidouterine fistula have previously appeared in the literature.

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TREATMENT OF AMEBIASIS WITH CAMOFORM

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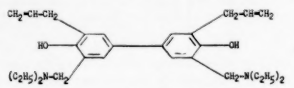
Laboratory evidence indicates that Camoform [biallylamicol, PAA-701, SN 6771, 6,6′-diallyl-α, α′-bis-(diethylamino)-4,4′-bi-o-cresol dihydrochloride] is effective against Entamoeba histolytica in vitro. Adcysts. Extraintestinal lesions also showed a good response. The authors recommend its use "as a prophylactic agent for dysenteric contacts." In India, Majumbar [7] obtained successful clinical and parasitological cure in 12 of 13 cases of amebiasis. In Egypt, Shafei [8] cured 10 of 15 patients with one course of treatment and a further 2 patients with a second course. Basmadji [9] in Iran treated two groups of patients. The first consisted of 14 patients, 72% of whom had negative stools 15 days after treatment, 70% after one month and 50% after three months. In a second series of 14 patients, all had negative stools five days after treatment, 64.3% after one month, and 50% after three months.



Structural formula of Camoform.

ministered orally to animals infected with E. histolytica, the drug is effective against intestinal amebiasis in rats and dogs, and amebic hepatitis in hamsters. Prophylactic oral administration of the drug confers protection against hepatic and pulmonary amebiasis in hamsters. The drug is also relatively nontoxic in animals after short-term administration, is rapidly absorbed, is stored in high concentration in the liver and lung (the most frequent sites of extraintestinal amebiasis), and is slowly excreted largely by way of the bile (resulting in prolonged fecal levels).[1]

Clinically it has been shown in a previous paper [2] to produce a rapid therapeutic response and cure in 82 of 85 patients with acute amebic colitis. Among 145 chronic cases, 112 were completely cured with one course of treatment, and 29 of the remaining 33 were cured with a second course of treatment. Hoekenga and Batterton [3] treated 10 patients with acute dysentery and 10 others with relatively asymptomatic infections. An 85% rate of apparent cure was obtained with a single course of treatment, and two of the three in whom treatment failed were cured when the treatment was repeated. Rapid clinical improvement was observed. The drug was well tolerated in each of these studies. Barrios [4] treated 16 cases of active amebic dysentery with apparent cure in each patient.

Milloy [5] administered Camoform to 36 patients suffering from chronic amebiasis who had previously been untreated. Twenty-three responded to therapy, six were unimproved, and in seven others treatment was stopped owing to aggravation of existing abdominal symptoms. Of 28 patients previously treated with other drugs, 5 did better on therapy with Camoform than with other drugs, in 12 the response was about the same, and 11 were unimproved. He concluded: "Camoform is especially advantageous in the treatment of chronic amebiasis as it can be given in small dosage over long periods of time without untoward symptoms."

In East Africa, De Mello and De Mello [6] treated 92 patients suffering from acute and chronic amebiasis, including 3 patients with amebic hepatitis. The symptoms were rapidly alleviated, and Camoform was effective in clearing the intestines of amebas and

Material and Methods

Thirty-nine patients suffering from chronic amebic dysentery confirmed by stool examination and one patient with pulmonary amebiasis were treated in this study. A dosage varying between 250 and 500 mg. of Camoform (1 to 2 tablets) three times a day was administered with meals. The drug was given with meals since administration afterwards had previously been found to lead to gastric intolerance. The course of therapy was continued for five days (15 doses). In addition to these 40 confirmed cases of amebiasis, 22 cases of dysentery diagnosed clinically as amebiasis but not confirmed by the isolation of E. histolytica were treated.

Results

In all cases there was symptomatic cure and the patient remained well over the subsequent several months of observation. All cases became free of E. histolytica after one course of treatment and there were no immediate relapses. It was also found that Camoform had a pronounced effect on E. coli, Chilomastix mesnili, Indolimax nana, Giardia lamblia, and Trichomonas hominis. After the course of treatment the occurrence of these protozoa was significantly reduced.

Treatment of a case of pulmonary amebiasis resulted in rapid termination of symptoms and radiologic and parasitological cure.

Report of a Case

The patient was a 60-year-old merchant with a history of an attack of colitis five years previously which had been cured in eight days without medical treatment. The sudden onset of a cough associated with fever and nausea were the reasons for his seeking medical attention. On the second day of observation he developed a brown expectoration and chest pain. On the third day he had the sensation of a foreign body in his chest. An x-ray showed an abscess, and E. histolytica was isolated from his sputum. Amebic pulmonary abscess was diagnosed and 750 mg. of Camoform was given daily for six days together with four injections of 400,000 units of penicillin. On the fourth day the general malaise, fever, and cough diminished

and only a slight cough remained on the sixth day. The patient felt well enough to leave his bed the following day, and his general condition was excellent. Two subsequent sputum analyses on the 10th and 13th days from the beginning of the illness were negative for E. histolytica, and an x-ray taken on the 29th day showed that the cavitation caused by the abscess had disappeared and appeared to be filled with sclerous tissue. The patient was seen again after two and one-half months, at which time he was in good condition.

Side-effects

Camoform was well tolerated by the majority of the patients, although a few suffered from occasional nausea, vomiting, and abdominal distress. The symptoms were not sufficiently severe to merit discontinuance of treatment in any patient and the side-effects subsided on completion of the course of treatment.

Summary

Forty patients with confirmed cases of amebiasis, including one patient with pulmonary amebiasis, were treated with Camoform with symptomatic and parasitological cure. No relapses occurred in the subsequent several months of follow-up. Side-effects were minimal and were in no cases sufficient to discontinue treatment.

This paper was translated from the original by Dr. Eugene H. Payne, 656 Van Dyke St., Detroit 14.

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CLINICAL EVALUATION OF ZOXAZOLAMINE (FLEXIN) IN CHILDREN WITH CEREBRAL PALSY

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and
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In an attempt to study the effect of zoxazolamine (Flexin) on children with cerebral palsy, we deemed a purely objective method of evaluation to be most advisable. Ninety-five children were selected at random, of whom 68 were spastics and 27 were athetoids. The diagnosis had been made by one or both of us. The youngest child was 2 years and 1 month of age and the oldest was 17 years. There was one adult, 28 years of age. The mean age was 8 years and 1 month (table 1).

There was a random distribution between the experimental and control groups with respect to intelligence levels, bracing, seizures, and whether the child was on therapy at the time of evaluation. Since these factors were randomly distributed, they were not considered to be of significance in the comparison of the experimental and control groups. If the child was on therapy, no effort was made to improve the test areas per se.

The drug was tested for its effect on the stretch reflex, i. e., the point at which the stretch reflex was elicited, and range of motion, including passive motion, active motion, and motion against resistance (or the ability to extend the flexed knee against weight). Weights of 3 lb. were used for children up to 5 years of age and of 5 lb. for those over 5. These tests were carried out on the biceps, triceps, quadriceps, and hamstring muscles, with the exception of motion against resistance, which was limited to the quadriceps. A specially designed goniometer, which recorded and marked the maximum point of motion, was used for the measurements.

The children were further evaluated as to their ability to perform an already learned task in a given length of time. These activities consisted of removing

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as many rings as possible from a peg in 60 seconds with each hand and with both hands and of putting as many blocks as possible in a box in 60 seconds with each hand and with both hands. Those who were ambulatory were checked as to the number of stairs they were able to climb in 60 seconds; in this functional test each child served as his own control.

The muscles of speech articulation were tested by determining the number of tongue-tip elevations, tongue lateralizations, jaw closures, and lip closures the child could perform in 10 seconds. Each child was evaluated in the areas outlined before medication, after one week of medication, and after four weeks of medication.

Drug Dosage

All children except those receiving the placebo, regardless of age or weight, were given one 250-mg. tablet of zoxazolamine orally three times daily with meals. This was continued for one week. Because of the early influx of complaints about dizziness, hypotonia, and rash among the smaller children, the dosage for all those from 3 to 5 years of age was decreased to 125 mg. three times daily with meals.

TABLE 1.—*Type of Cerebral Palsy, Drug Administered, and Ages of Ninety-five Children in Whom Zoxazolamine Was Studied*

Type of Cerebral Palsy	Location	Drug Received	Patients, No.	Age, Yr., Mo. Mean	Range
Athetoid		Zoxazolamine	19	9,4	2,1-17,2
		Placebo	8	8,5	2,1-14,0
Spastic	Hemiplegia	Zoxazolamine	15	7,2	3,2-13,4
		Placebo	7	7,3	2,6-13,6
Spastic	Mixed	Zoxazolamine	13	7,7	3,4-13,6
		Placebo	5	8,3	4,7-14,1
Spastic	Quadriplegia	Zoxazolamine	21	5,6	2,6-28,5
		Placebo	7	8,5	3,1-12,9
Spastic, total group		Zoxazolamine	49	7,6	2,6-28,5*
		Placebo	19	8,0	2,6-14,1
Total group		Zoxazolamine	68	8,1	2,1-28,5†
		Placebo	27	8,1	2,1-14,1

* Next youngest patient was 13 yr., 6 mo.
† Next youngest patient was 17 yr., 2 mo.

These doses were maintained for the remaining three weeks of the test period. In no child was medication discontinued.

Sixty-eight children were given zoxazolamine and 27 were given a placebo. Of the 68 spastics, 49 received the drug and 9 the placebo. Of the 27 athetoids, 19 received the drug and 8 the placebo. Reactions were few. Three children developed a rash; one, nasal stuffiness; one, dizziness; two, headache; four, drowsiness; and one, hypotonia. This was a total of nine children, since two complained of both headache and drowsiness; one of these patients was receiving the placebo. Determinations of the hemoglobin level and leukocyte and differential counts were done on all children before the test and on the experimental group at the end of the test period. There was no effect on the hemoglobin level or the white blood cell or differential counts.

Results

An analysis of the results in the individual test areas is shown in tables 2 through 7. When the t-test was applied to the results it showed that there was no significant difference between the improvement obtained in the experimental group and that in the control or placebo group.

TABLE 2.—*Improvement in Stretch Reflex After Medication in Children with Cerebral Palsy Receiving Zoxazolamine or a Placebo*

Type and Location of Cerebral Palsy	Muscle Tested	Mean Improvement* in Drug Group†	P‡	Mean Improvement* in Control Group†	Significance of Difference§
Spastic, mixed	Right hamstrings	10	0.01	Not known	...
Spastic, quadriplegia	Left hamstrings	10	0.03	Not known	...
Spastic, total group	Hamstrings	9	0.05	8	None

* Improvement measured in degrees of arc.
† Drug group received zoxazolamine, control group received placebo.
‡ P=probability that observed improvement in drug group was due to accident of sampling.
§ Significance of difference between improvement in drug group and that in control group.

The stretch reflex was improved in the hamstring muscles of the spastic patients only, the mean improvement ranging from 9 to 10 degrees of arc (table 2). This improvement was not significantly different from that in the placebo group. Passive range of motion was improved in the quadriceps, hamstring muscles, and biceps of the spastics and athetoids, the mean improvement ranging from 3 degrees of arc for the biceps of the spastic patients with hemiplegia to 12 degrees of arc for the right hamstring muscles of the spastic patients with quadriplegia (table 3). This improvement did not vary significantly from that in the control group.

TABLE 3.—*Improvement in Passive Range of Motion After Medication in Children with Cerebral Palsy Receiving Zoxazolamine or a Placebo*

Type and Location of Cerebral Palsy	Muscle Tested	Mean Improvement* in Drug Group†	P‡	Mean Improvement* in Control Group†	Significance of Difference§
Spastic, hemiplegia	Biceps	3	0.04	3	None
Spastic, quadriplegia	Right biceps	5	0.01	10	None
	Left biceps	7	0.01	7	None
	Left quadriceps	11	0.03	Not known	...
	Right hamstrings	12	0.05	18	None
	Left hamstrings	9	0.01	9	None
Spastic, total group	Biceps	4	0.01	7	None
	Hamstrings	6	0.02	11	None
	Left hamstrings	6	0.05	11	None
Athetoid	Right hamstrings	9	0.01	0	None
	Right biceps	5	0.01	-6	0.01

* Improvement measured in degrees of arc.
† Drug group received zoxazolamine, control group received placebo.
‡ P=probability that observed improvement in drug group was due to accident of sampling.
§ Significance of difference between improvement in drug group and that in control group.

Active range of motion was improved in the hamstring muscles, biceps, and triceps of the spastics and athetoids from 7 to 22 degrees of arc, but not more significantly than in the control group (table 4). Resistance, or ability to extend the knee against a constant weight of 3 or 5 lb., was tested on the quadriceps only, and the spastics and the athetoids showed a range of mean improvement of 9 to 13 degrees of arc, which was not significantly different from the mean improvement in the control group (table 5).

For hand and arm skills (rings off peg, blocks in the box), the spastic group alone showed a mean increase of one to five actions in 60 seconds (table 6). This was not significantly different from the mean improvement of the control group. In functional work, specifically stair climbing, the spastic group alone showed a mean increase of four steps in 60 seconds. No significant difference from the improvement in the control group was found (table 6). The tests for the muscles involved in speech articulation (tongue elevation and lateralization, lip and jaw closures) in the spastics and athetoids showed a mean increase in the number of motions performed of from 2 to 10 in 10 seconds (table 7). There was no significant difference between this mean and that for the control group.

TABLE 4.—*Improvement in Active Range of Motion After Medication in Children with Cerebral Palsy Receiving Zoxazolamine or a Placebo*

Type and Location of Cerebral Palsy	Muscle Tested	Mean Improvement* in Drug Group†	P‡	Mean Improvement* in Control Group†	Significance of Differences§
Spastic, hemiplegia	Triceps	8	0.04	10	None
Spastic, quadriplegia	Left biceps	13	0.01	8	None
	Right hamstrings	22	0.02	11	None
Spastic, total group	Hamstrings	11	0.01	11	None
	Biceps	9	0.03	8	None
	Triceps	9	0.01	14	None
Athetoid	Right hamstrings	7	0.05	9	None
	Left hamstrings	9	0.03	11	None

* Improvement measured in degrees of arc.
† Drug group received zoxazolamine, control group received placebo.
‡ P=probability that observed improvement in drug group was due to accident of sampling.
§ Significance of difference between improvement in drug group and that in control group.

TABLE 5.—*Improvement in Motion Against Resistance After Medication in Children with Cerebral Palsy Receiving Zoxazolamine or a Placebo*

Type and Location of Cerebral Palsy	Muscle Tested	Mean Improvement* in Drug Group†	P‡	Mean Improvement* in Control Group†	Significance of Differences§
Spastic, quadriplegia	Right quadriceps	12	0.01	10	None
	Left quadriceps	11	0.01	5	None
Spastic, mixed	Right quadriceps	10	0.03	Not known	...
	Left quadriceps	10	0.02	Not known	...
Spastic, total group	Quadriceps	9	0.01	4	None
Athetoid	Right quadriceps	13	0.04	Not known	...

* Improvement measured in degrees of arc.
† Drug group received zoxazolamine, control group received placebo.
‡ P=probability that observed improvement in drug group was due to accident of sampling.
§ Significance of difference between improvement in drug group and that in control group.

TABLE 6.—*Improvement in Functional Hand and Arm Skills After Medication in Children with Cerebral Palsy Receiving Zoxazolamine or a Placebo*

Type and Location of Cerebral Palsy	Activity	Mean Improvement* in Drug Group†	P‡	Mean Improvement* in Control Group†	Significance of Differences§
Spastic, hemiplegia	Rings off peg (both hands)	5	0.01	5	None
Spastic, quadriplegia	Rings off peg (both hands)	2	0.01	1	None
Spastic, total group	Rings off peg (both hands)	3	0.01	3	None
	Rings off peg (one hand)	1	0.04	2	None
	Blocks in box (one hand)	2	0.01	1	None
	Stair climbing	4	0.05	7	None

* Improvement measured as increase in number of times activity could be performed in 60 seconds.
† Drug group received zoxazolamine, control group received placebo.
‡ P=probability that observed improvement in drug group was due to accident of sampling.
§ Significance of difference between improvement in drug group and that in control group.

TABLE 7.—*Improvement in Use of Muscles of Speech Articulation After Medication in Children with Cerebral Palsy Receiving Zoxazolamine or a Placebo*

Type and Location of Cerebral Palsy	Activity	Mean Improvement* in Drug Group†	P‡	Mean Improvement* in Control Group†	Significance of Differences§
Spastic, hemiplegia	Jaw closure	3	0.05	0	None
Spastic, quadriplegia	Jaw closure	2	0.05	7	None
Spastic, mixed	Jaw closure	4	0.01	Not known	...
Spastic, total group	Jaw closure	3	0.01	3	None
Athetoid	Jaw closure	3	0.02	Not known	...
Spastic, hemiplegia	Lip closure	4	0.01	0	None
Spastic, quadriplegia	Lip closure	3	0.01	5	None
Spastic, mixed	Lip closure	4	0.01	Not known	...
Spastic, total group	Lip closure	4	0.01	3	None
Athetoid	Lip closure	5	0.01	Not known	...
Spastic, quadriplegia	Tongue elevation	3	0.01	5	None
Spastic, total group	Tongue elevation	3	0.01	3	None
Athetoid	Tongue elevation	2	0.02	Not known	...
Spastic, hemiplegia	Tongue lateralization	3	0.05	6	None
Spastic, total group	Tongue lateralization	2	0.01	5	None

* Improvement measured as increase in number of times activity could be performed in 10 seconds.
† Drug group received zoxazolamine, control group received placebo.
‡ P=probability that observed improvement in drug group was due to accident of sampling.
§ Significance of difference between improvement in drug group and that in control group.

Table 8 summarizes the data concerning all areas tested in which there was significant improvement after medication and again points out that in no case was the improvement in the drug group significantly greater than that in the control group. In fact, in looking at the individual tables we see

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that, although the mean difference between the improvement in the experimental group and that in the control group is not of significance when viewed statistically, the control (placebo) group in many instances showed a greater range of improvement than the experimental group.

Subjective Reports from Parents

The therapists, the parents, the patients, and one of the doctors did not know which children received zoxazolamine and which the placebo. Upon completion of the evaluations, subjective reports were requested from the parents. Forty-eight replies were received from the parents of the 68 children receiving zoxazolamine. Twenty-five reported improvement, 16 reported no effect, and 8 reported bad effects. The improvements noted were as follows: 16 children were more relaxed, 9 showed functional improvement, and 9 were sleeping better. In some individuals more than one area of improvement was noted.

Seventeen replies were obtained from the parents of the 27 children receiving the placebo. Ten noted improvement, 4 noted no effect, and 3 noted ill-effects. Five children were more relaxed, six showed functional improvement, and one slept better.

Conclusions

Although the preliminary pilot studies [1] seemed to indicate the efficacy of zoxazolamine in the treatment of cerebral palsy, this particular study does not demonstrate any appreciable effect, in the dosage in which the drug was used, on the stretch reflex; on the range of motion, either passive, active, or against resistance; or upon performance of an already learned task. We endeavored to approach the problem purely objectively. The only real variable in the results is apparently psychological.

We do not presume to say that the drug is without effect. Perhaps an increase in dosage and intensive work with the child during the period of administration might bring about some improvement. But the drug alone is not the answer for the treatment of cerebral palsy, as no drug has been to date. Hard work, proper and adequate bracing, and judicious surgery, coupled with normal growth and an opportunity for maturation, still give the best results.

TABLE 8.—*Summary of Data Concerning Areas in Which There Was Significant* Improvement After Medication in Children with Cerebral Palsy Receiving Zoxazolamine or a Placebo*

Function Tested	Muscles or Activity Tested	Type and Location of Cerebral Palsy	No. of Children in Drug Group†	No. of Children in Control Group†	Mean Improvement in Drug Group, Range	Significance of Difference‡
Stretch reflex	Hamstrings	Spastic, quadriplegia	14	5		
		Spastic, mixed	12	5	9-10§	None
		Spastic, total group	41	18		
Passive range of motion	Quadriceps, hamstrings, biceps	Spastic, hemiplegia	15	7		
		Spastic, quadriplegia	12-19	2-7		
		Spastic, total group	37-47	17-19	3-12§	None
		Athetoid	19	8		
Active range of motion	Hamstrings, biceps, triceps	Spastic, hemiplegia	11	4		
		Spastic, quadriplegia	18	7	7-22§	None
		Spastic, total group	24-46	6-20		
		Athetoid	18	8		
Motion against resistance	Quadriceps (only one tested)	Spastic, quadriplegia	14-16	5	9-13§	None
		Spastic, mixed	12	5		
		Spastic, total group	41	15		
		Athetoid	11	4		
Hand and arm skills	Rings off peg, blocks in box	Spastic, hemiplegia	15	6		
		Spastic, quadriplegia	16	5	1-5‖	None
		Spastic, total group	33-36	13		
Functional work	Stair climbing	Spastic, total group	22	9	4‖	None
Speech articulation	Motion of tongue, lips, jaw	Spastic, hemiplegia	11-12	5-6		
		Spastic, quadriplegia	13-17	5		
		Spastic, mixed	12	4	2-5¶	None
		Spastic, total group	33-41	13-15		
		Athetoid	13-15	6		

* Probability that improvement in drug group was due to accident of sampling was 0.1 to 0.5.
† Drug group received zoxazolamine, control group received placebo.
‡ Significance of difference between improvement in drug group and that in control group.
§ Improvement measured in degrees of arc.
‖ Improvement measured as increase in number of times activity could be performed in 60 seconds.
¶ Improvement measured as increase in number of times activity could be performed in 10 seconds.

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SPECIAL ARTICLE

SOCIAL SECURITY FOR PHYSICIANS

2. POSITION OF THE MEDICAL PROFESSION CONCERNING THE COVERAGE OF PHYSICIANS UNDER THE SOCIAL SECURITY ACT

The American Medical Association, through repeated actions of its House of Delegates and Board of Trustees, has expressed its opposition to the compulsory coverage of physicians under Title II (Old Age, Survivors and Disability Insurance Provisions) of the Social Security Act. The Association is not opposed to the voluntary inclusion of physicians under this title of the act.

Eight years ago, in June, 1949, at Atlantic City, the House of Delegates adopted a resolution disapproving the extension of "Social Security" to self-employed individuals including physicians.

In December, 1953, the House again opposed such coverage. In June, 1954, 1955, and 1956, the House reaffirmed its opposition to the compulsory coverage of physicians under the Social Security Act. In June, 1954, the Board of Trustees enlarged upon the Association's position to indicate that there was no opposition to the coverage of physicians under the act on a voluntary basis.

In June, 1957, at New York, the House most recently reaffirmed its position on Social Security coverage and recommended a stepped-up information program to explain the reasons for the medical profession's position on this issue.

Reasons for the Medical Profession's Position

Many informed members of the profession have seen and are deeply concerned about the inevitable pattern of social insurance schemes. Their growth from retirement payments to survivorship payments to permanent and total disability payments to temporary cash sickness benefits and finally to national compulsory health insurance is all too clear. One nation after another has succumbed to the drive to extend the compulsory system of taxation called "social insurance" to finance a vast program of medical and hospital care for taxpayers and nontaxpayers. The history of developments in this field in foreign countries has, therefore, served to warn the medical profession in this country of the usual consequences of a federal social security program.

The Social Security Act in the United States, which was born of the depression in 1935, has followed this traditional pattern of expansion despite a period of continuing national prosperity. Contrary to the approach of those who suggest more and more federal benefits, the medical profession has continuously adhered to the philosophy that rewards by the federal government for long life create a leveling or an averaging process which, when combined with ever-increasing taxes, tend to destroy individual initiative and will result in increased federal control of and responsibility for an increasing percentage of our people.

In tracing the history of Social Security, it will be noted that the program has continuously been referred to as "insurance." This is a misnomer. In 1934, only a year before the Social Security Act became law, the United States Supreme Court rebuked the 73rd Congress for trying to avoid responsibility under the veterans' insurance contracts issued during World War I. With this decision fresh in their minds, the persons who drafted the Social Security Act were careful to see that nobody got a contract under Title II of that program.

Later, in 1937, the United States Attorney General in defending the constitutionality of the Social Security Act before the United States Supreme Court stated, "Social security benefits are gratuities to be paid by the national government directly to individuals. The Act creates no contractual obligation with respect to the payment of benefits." The entire program was, at that time, justified to the Supreme Court on the public-charity, general-welfare theory and on that basis, on May 24, 1937, the court upheld the constitutionality of the act. That decision established the legal character of Social Security.

The fact that the Social Security Act creates no contractual obligations with respect to the payment of benefits was again very frankly and honestly admitted in a report of December, 1954, issued by the Ways and Means Committee of the House of Representatives entitled "Social Security After Eighteen Years."

Thus, the law requires the payment of "premiums," but does not guarantee the payment of benefits in return. In addition, tax rates, the taxable wage base, and the type and amount of benefits are not stable, as demonstrated by the many changes legislated by Congress during the past 20 years. Finally, the benefits that are available are qualified by conditions with which most of the people who are being taxed are unfamiliar.

Is the Social Security program actuarially sound? According to normally accepted insurance standards the answer must be "no." The 1954 report of the House Ways and Means Committee, referred to above, spells out in detail the ratio of taxes paid

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to benefits received. The report states that retired eligible beneficiaries under the Old Age, Survivors and Disability Insurance program as of December, 1952, were receiving and will receive, on the average, benefits equal to $24 for each 50 cents paid in taxes during the working years of their lives. This ratio was further increased by the amendments of 1954 to $30 in benefits for each 50 cents paid in taxes. Figures following the 1956 amendments have not as yet been reported.

It is obvious that when the government provides something to an individual or to a group for less than it actually costs, part of the cost must be paid by someone else. These deficits will have to be met by higher Social Security taxes, through higher income taxes, or by reducing the benefits under the program.

Since most self-employed physicians do not retire at age 65, the compulsory tax which would be imposed upon them if they become covered under the Social Security system would be unjust and unreasonable. It is a proved fact that physicians who are able to work seem to prefer to keep right on practicing medicine. A survey on this point shows that over 85% of the doctors between the ages of 65 and 72 are in active practice. Over 50% of physicians who retire do so after the age of 74. Thus, if forced under this program, a typical physician would be required to continue to pay Social Security taxes until age 72 before he would receive benefits. This is true because of the work-test applied to retired covered employees described in the first article of this series.

Since Social Security retirement benefits are not of primary value to physicians, the taxes which they would pay under the program would be used primarily to finance any survivorship benefits which might accrue to the physician's family. The amount of these taxes is sufficient to purchase comparable survivorship benefits from private insurance companies.

For the aforementioned sound philosophical and economic reasons, the medical profession has opposed the compulsory coverage of its members under what it considers to be an unsound, unsuited, and unsolicited government welfare program.

COUNCIL ON DRUGS

Report to the Council

The Council has authorized publication of the following report.

H. D. KAUTZ, M.D., *Secretary.*

Because of the renewed awareness of genetics in relation to the cause of disease and because of an increasing interest in this subject, the following article is most timely. The author has prepared this report at the invitation of the Subcommittee on Blood Dyscrasias of the Committee on Research.

NORMAN DE NOSAQUO, M.D., *Secretary, Committee on Research.*

DRUG REACTIONS, ENZYMES, AND BIOCHEMICAL GENETICS

Arno G. Motulsky, M.D., Seattle

In discussions of drug idiosyncrasy, careful distinction should be made between toxic reactions caused by immunologic mechanisms (drug allergy) and abnormal reaction caused by exaggeration or diminution of the usual effect of a given dose.[1] Although some progress has been made in the study of mechanisms of drug allergy, little was known until recently about the pathogenesis of hypersusceptibility reactions and hyposusceptibility reactions. Data are available now which suggest that reactions of this type may be caused by otherwise innocuous genetic traits or enzyme deficiencies.

From the Department of Medicine, University of Washington Medical School. Dr. Motulsky is a John and Mary R. Markle Scholar in Medical Science.

Hockwald and his co-workers [2] demonstrated that approximately 10% of American Negroes and a very small number of caucasians developed hemolytic anemia when given an average dose of primaquine or chemically related drugs. Beutler and associates [3] showed that red blood cells of susceptible individuals possessed decreased numbers of nonprotein, sulfhydryl groups. It has now been pointed out that primaquine sensitivity is related to glucose-6-phosphate dehydrogenase activity.[4] Investigations of the genetics of this trait, now in progress, suggest that the abnormality is caused by a sex-linked gene of intermediate dominance.[5] The red blood cell abnormality per se has no known deleterious effect on the individual or on red blood cell life span. Excessive doses

of primaquine or related drugs appear to produce hemolytic anemia in all individuals. The red blood cells of susceptible subjects lack sufficient enzymatic protection against damage by the drug even with smaller dosage levels. These investigations explain the greater incidence of hemolytic anemia among Negroes when they were given pamaquine or sulfanilamide in past years. Hemolytic anemia due to naphthalene [5] and nitrofurantoin (Furadantin) [6] also has been demonstrated to be associated with the sulfhydryl defect responsible for primaquine sensitivity. Two different in vitro tests to detect susceptibility have been described.[7]

Lehmann and Ryan [8] pointed out that prolonged apnea caused by the muscle relaxant succinylcholine (Anectine, Quelicin, Sucostrin) chloride sometimes can be explained by low levels of pseudocholinesterase. A certain amount of this enzyme is required for inactivation of the drug. The enzyme was found to be diminished in sensitive patients as well as in some of their family members. These findings have been confirmed.[9] The exact mode of inheritance of this familial enzymatic deficiency is still indeterminate. Other causes of pseudocholinesterase deficiency such as malnutrition and liver diseases were ruled out.

It is not unlikely that some drug sensitivity reactions previously characterized as caused by hypersusceptibility may be produced by similar mechanisms. It is also possible that the potential for antibody formation due to haptenes, and therefore susceptibility to drug allergy, is conditioned by genetic factors. Knowledge of the metabolic fate of various drugs and improved methods of studying enzyme and antibody reactions in man promise to provide tools for further approaches to this problem.

Patients with hereditary hyperbilirubinemia (constitutional nonhemolytic jaundice) are likely to be a challenging group for study, since they have been postulated to have deficient enzymatic machinery for the coupling of bilirubin to glucuronides.[10] Since many drugs such as salicylates and sex hormones are excreted as glucuronides, valuable hints may be forthcoming from study of the fate of such drugs in these patients. The precipitation of symptoms of acute intermittent porphyria by barbiturates and alcohol is well known. Further evidence of interference by these agents with the disordered enzymatic reactions responsible for the disease is likely to be found. Megaloblastic anemia is sometimes produced by anticonvulsants.[11] A genetically determined abnormality of folic acid metabolism may be the reason for this complication. Liver damage caused by cinchophen, jaundice induced by chlorpromazine, and cinchonism produced by small doses of quinine or quinidine are other reactions possibly caused by genetic enzymatic defects.

Tolerance to drugs or failure of expected effect with an average dose may have a similar basis. No proved examples due to genetic defects exist in man. Some strains of rabbits, however, can be given large quantities of atropine and related compounds without effect.[12] These animals inactivate atropine by a genetically controlled enzyme, atropinesterase, in the blood and tissues. Marked variability in length of narcosis induced by hexobarbital (Evipal) sodium has been described in various species and in different strains within a species. These differences could be related to variable enzymatic detoxification activity in liver microsomes.[13] Insulin-resistant mouse strains exist which survive 300 times the dose of insulin which kills normal mice.[14]

Qualitative differences between species also exist. A drug effect exhibited by most individuals of one species may be rare in other species. Thus, hyperexcitability due to morphine is the usual response in cats and race horses but occurs rarely in man in whom it is considered an idiosyncrasy. Comparative biochemical studies on drug metabolism may provide clues to such idiosyncrasies.

Another pertinent area for research includes drug reactions involving red blood cell constituents in the newborn. Toxic methemoglobinemia is produced in this age period by exposure to aniline dye-stamped diapers [15] or by ingestion of well-water high in nitrate content.[16] Over 90% of the well-water cases have occurred in children under two months of age.[17] Since the concentration of the red blood cell enzyme required for reduction of methemoglobin to hemoglobin is decreased in the red blood cells of the newborn,[18] it is probable that such enzyme deficiency provides a partial explanation for the maintenance of the abnormal pigment. Red blood cell destruction by excessive doses of menadiol sodium diphosphate (Synkayvite Sodium Diphosphate, Vitamin K Analogue) caused hemolytic anemia and kernicterus in some infants and has been related to low vitamin E levels in cells of infants.[19] The lowered concentration of red blood cell catalase in cells of infants [20] may be one significant factor in susceptibility to vitamin K hemolysis. The previously mentioned sulfhydryl defect associated with a variety of drug sensitivities also may predispose the infant to vitamin K hemolysis.[5]

The detection of hereditary biochemical traits that cause drug reactions may contribute to the progress of human genetics in general. Such traits may be related to susceptibility or resistance to diseases other than drug idiosyncracies. Some geneticists argue that relatively rare traits such as some of those under discussion could not be maintained in the population at their observed frequency unless such traits provided the carriers with some selective advantage.[21] The general validity of this argument appears to have been confirmed by the demonstration of decreased malaria mortality in infants with sickle-trait and the possible relationship of the ABO blood groups to the frequency of diseases such as ulcer and gastric cancer.

Since a given gene may be more frequent in certain ethnic groups, any drug reaction that is more frequently observed in a given racial group, when other environmental variables are equal, will usually have a genetic basis. Investigations on drug reactions there-

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fore should include careful notation of the ethnic or racial extraction of the patient. Consanguinity, such as in first-cousin marriages among the parents, points to a recessive genetic mechanism and should be inquired about and mentioned. Unfortunately, drug reactions among parents and siblings will not often be elicited when the physician is taking a family history, because families are small and most drugs are new and have not been used for long. Once a possible hereditary defect is identified, family and population surveys are desirable.

Genetically conditioned drug reactions not only are of practical significance but may be considered pertinent models for demonstrating the interaction of heredity and environment in the pathogenesis of disease. In these instances it can be shown clearly how hereditary, gene-controlled enzymatic factors determine why, with identical exposure, certain individuals become "sick," whereas others are not affected. It is becoming increasingly probable that many of our common diseases depend on genetic-susceptibility determinants of this type. Haldane's prediction [22] that "the future of biochemical genetics applied to medicine is largely in the study of diatheses and idiosyncrasies, differences of innate make-up which do not necessarily lead to disease but may do so" has been confirmed by these recent developments in therapeutics.

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Sedation Threshold.—Several recent neurophysiological advances, such as the elucidation of reticular system functions, seem highly relevant to the understanding of brain mechanisms involved in psychological disorders. Most of this information has come from the animal laboratory or from patients subjected to surgical operations. Pertinent methods for neurophysiological study of the intact human subject are needed to provide closer links between the data of the psychiatric clinic and the neurophysiology laboratory. This paper deals with one such method, the sedation threshold. The sedation threshold is an objective pharmacological determination, which depends upon the electroencephalographic (EEG) and speech changes produced by intravenous Sodium Amytal. Starting from the common clinical impression that effect sedative dosage is correlated with the degree of tension, the method was originally developed to measure tension or manifest anxiety. After the realization of this initial aim, continued research revealed additional psychological correlates of the sedation threshold. The results indicated that the method has important potentialities as a tool in psychiatric and psychomatic research.—C. Shagass, M.D., Sedation Threshold, *Psychosomatic Medicine*, September-October, 1956.

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DIAGNOSIS OF URINARY TRACT INFECTION

WITH the publication in this issue (page 815) of the report by Clabaugh and Rhoads, the subject of the diagnosis of urinary tract infections is reopened. The finding of potentially pathogenic organisms in a so-called clean specimen of urine, although suggestive of such an infection, is far from being conclusive evidence of it. Guze and Beeson,[1] quoted by these authors, found that despite use of careful aseptic and antiseptic technique some bacteria were transferred from the urethra to the bladder during catheterization and concluded that obtaining a specimen of urine in this way does not provide a completely trustworthy specimen for bacteriological culture. Even though the urinary meatus is scrupulously cleaned, organisms comprising what may be considered the normal urethral flora remain in the anterior portion of the urethra. Philpot[2] investigated the flora of the so-called clean or midstream voided urine of normal men and catheterized specimens from normal women and found that 82% of the former and 34% of the latter contained bacteria, many of which were potential pathogens. Because these subjects had no symptoms suggestive of urinary tract infection, he concluded that the finding of such organisms in the urine does not necessarily indicate the presence of a bacterial disease. In most subjects these organisms although present were few in number. This suggests that the number of bacteria present is probably as important as their identification. This conclusion was further borne out by MacDonald and co-workers,[3] who believe that counts of more than 100,000 organisms per cubic centimeter of uncentrifuged urine indicate active urinary tract infection. Philpot believes that any organism seen in a direct smear of uncentrifuged urine stained by Gram's method is probably present in numbers of 100,000 per cubic centimeter or more.

Clabaugh and Rhoads, by using a catheter within a catheter, observed positive cultures in 52% of urine specimens obtained through the larger catheter and 32% in those obtained from the smaller catheter. Broth cultures in which the catheter tips were dipped after removal were positive in 89% in the case of the larger catheters and 52% in the case of the smaller. These were all from female patients who, although most of them were asymptomatic, all showed the presence of leukocytes in the urine and were believed to have some degree of urinary tract infection. Theoretically even with this technique it is possible to introduce urethral contaminants into the bladder, but the likelihood of this is greatly reduced. Further studies on this possibility should be made. There is a great need for a sharpening of the diagnostic procedures used to determine urinary tract infections because many patients who do not need such treatment are treated for this condition on the basis of a positive culture of a catheterized specimen obtained in the usual way. If the new technique results in fewer cases of cystitis due to instrumentation, this will be an added boon.

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WHAT PRICE ACCIDENTS?

Elsewhere in this issue (page 846) is a summary by the Bureau of Medical Economic Research of the American Medical Association of its nationwide survey of the burden of patients hospitalized on account of accidents. The summary offers several criteria for measuring the accident load. For example, payroll expenses of these hospitals because of accident cases in 1955 were 198 million dollars, or 7.3% of the total payroll. In general, the burden of accident cases is 7 to 8% of the grand total for the 6,000 general and special hospitals in the United States. Presumably, the burden on physicians comes within the same range. The proportion of cases treated by physicians in the home and the office in the accident category will be estimated in later bulletins in this series. The National Safety Council has utilized earlier studies of the Bureau of Medical Economic Research—notably, the finding that fatal accidents outrank heart disease, whose special victims are retired persons, as the number 1 destroyer of the working years of life in the United States. Moreover, these new findings, in addition to others in this series of studies by the Bureau of Medical Economic Research, clearly establish that accidents and the other great nondisease category, pregnancy, together account for about one-fourth of the aggregate hospital load. It is most unfortunate that many careless observers infer that patients in disease categories comprise 100% of the national hospital burden.

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ORGANIZATION SECTION

JUDICIAL COUNCIL SESSION

Two appeals alleging discrimination against medical society membership were heard in Chicago last month by the A. M. A. Judicial Council. In one case the Council determined it was powerless to act, for lack of jurisdiction. The other appeal was turned down for lack of "convincing proof of irregularity"—but with a recommendation that the A. M. A. Board of Trustees create a special committee to help bring agreement out of an underlying dispute.

In other actions, the Judicial Council rendered its first interpretive opinion involving the newly worded A. M. A. Principles of Medical Ethics and submitted an annual report. (Detailed reports on the Sept. 7 meeting will be published in later issues of THE JOURNAL.)

Georgia Case

A special committee of trustees was suggested to help settle differences between the Medical Association of Georgia and the Richmond County, Ga., Medical Society on one hand, and six salaried physicians on the other hand. These doctors are faculty members of the Medical College of Georgia and practice at the college's Talmadge Memorial Hospital. They claim they are being refused medical society membership because they accept fees for treating private patients in the hospital. All these fees go into a hospital research fund.

The county and state medical associations contended that the six physicians are engaged in corporate practice of medicine, in violation of medical ethics, because a contract specifying disposition of the fees does not allow the physicians unrestricted choice of how the money will be spent. Both sides expressed hope for an early solution to the problem. As Dr. George R. Dillinger, chairman of the council of the Medical Association of Georgia, told the A. M. A. Council: "We only want the problem settled ethically and legally."

Colorado Case

The Council ruled lack of jurisdiction in the case of Dr. William D. Broxon of Trinidad, Colo. He argued that the Las Animas County Medical Society threatened to label him as unethical unless he withdrew his association with the United Mine Workers of America health and welfare fund. He claimed inadequate response to an appeal to the Colorado State Medical Society—whose representatives testified that the society had taken no improper actions against Dr. Broxon, and that the U. M. W. A. was not a factor in the case. The Judicial Council members agreed that, since there were no actual charges against Dr. Broxon and since he was a county society member in good standing, they had no issues upon which to rule.

Local Responsibility

In its annual report the Council reaffirmed its stand that local medical societies should accept responsibility in deciding judicial matters affecting their own members. A local medical society ethics committee, noted the Council, is "a body before whom the accused could appear, hear the charges brought against him and offer his defense. While it is never pleasant to find a colleague guilty and impose punishment this is a responsibility falling on some of us. Local committees charged with hearing complaints alleging unethical conduct are under no obligation to find every accused guilty."

But, the Judicial Council went on to say: "If local societies fail to curtail unethical practices, ethics lose their effectiveness. Failure on the part of the component society to demand respect for and adherence to the Principles [of medical ethics] breeds contempt and disrespect for them."

Opinion on Ethics Principles

The Judicial Council's first interpretive opinion on the Principles as revised last June was given in reply to a question of K. C. Young, executive secretary of the Los Angeles County Medical Association. He quoted Item 7, which states that a physician's fee "should be commensurate with the services rendered and the patient's ability to pay." Young asked whether this means that a physician is authorized to double his fee if the patient's income is twice that of the average person, and if the fee should be scaled down accordingly for patients with below-average income. He wrote: "An opinion on this point is particularly needed by our fee complaint committee, which in the past have largely given opinions based on an average fee."

The Council emphasized that the "basic ethical concepts" included in both the 1955 and 1957 editions of the Principles are identical in spite of changes in format and wording. "Therefore," it stated, "no opinion or report of the Council interpreting these basic principles which were in effect at the time of the revision has been rescinded by the adoption of the 1957 Principles." The Council replied to Young that Section 7 of the Principles "does not imply or mean that a sliding scale of fees is to be adopted individually or by the profession . . . to justify an excessively high fee or to approve

an inadequately low fee." Said the Judicial Council: "[The phrase] 'commensurate with the services rendered' recognizes that although there are some services which are considered invaluable, nonetheless their practical value lies within a range—within limits above or below which a fee is unconscionable." The opinion also pointed out that the doctor-patient advance discussion of fees will solve most related problems before they occur.

Chairman of the Judicial Council is Dr. Homer L. Pearson Jr., of Miami. Other members are Drs. George A. Woodhouse of Pleasant Hill, Ohio; James M. Hutcheson of Richmond, Va.; Louis A. Buie Sr., of Rochester, Minn.; and Robertson Ward of San Francisco.

MEDICINE-TELEVISION RESPONSE IN WAUSAU, WIS.

Another success story in medical public relations via television station liaison (THE JOURNAL, May 4, 1957, page 49) is being told in Wausau, Wis. The Marathon County Medical Society, with station FSAU-TV, reports "marvelous response" from viewers of regular Sunday half-hour live telecasts which began as a public service feature last June 16.

"If we can make one person in our area think about medicine and how it might be able to help him, we have accomplished our goal," said Bart Kellnhauser, WSAU-TV program director. The weekly series, entitled "Our Medical Service," combines a panel discussion (in lay terms) with questions from the viewing audience, medical equipment demonstrations, and a variety of visual materials. Recent programs have covered the separate topics of

Fig. 1.—Technician James Harrun demonstrates the taking of an electrocardiogram during weekly telecast presented as a public service by Marathon County Medical Society and WSAU-TV in Wausau, Wis. Medical student Kenneth Ender enacts role of patient.

poliomyelitis, first aid, cancer, auto safety, heart disease, civil defense, and hospitals. Scheduled for later presentation were mental health, medicine and religion, health and athletics, advances in surgery, the physician and world peace, medical education, and the doctor and the teen-ager.

Dr. Marvin H. Olson of Wittenberg, Wis., who directs the series and serves as moderator, said: "The volume of mail with questions and comments is gradually increasing, and the program has also been enthusiastically followed by the medical profession and allied groups. A thirteen-week series was originally scheduled but it has been decided to continue the program indefinitely, and plans are being made to increase the length to a full hour."

Fig. 2.—Drs. J. Struthers, J. M. Freeman, and M. H. Olson prepare for panel discussion which highlights program.

Individual telecasts are centered around a panel of three or four physicians invited by rotation through county society membership and, occasionally, from neighboring medical societies. One participating physician remarked that the program was the best thing that had happened around Wausau in a long time. Said Dr. Olson: "Viewers are acquiring a needed sense of security in knowing that their own doctors are able to make modern advances in medicine available to them. This is encouraging early treatment, and renewing and increasing their faith in their family physician."

A. M. A. CLINICAL MEETING IN PHILADELPHIA

Philadelphia will be the scene of the A. M. A. 11th Clinical Meeting on Dec. 3 through 6. The center of activities will be Convention Hall where scientific exhibits, color television, motion pictures, technical exhibits, and lectures will be presented. Headquarters for the House of Delegates will be at the Bellevue-Stratford Hotel.

The convention will be geared especially for family doctors. Some of the highlights include (1) transatlantic conference between distinguished physicians in London and Philadelphia on "Advances in Chemotherapy of Cancer" via two-way telephone, 3 p. m. EST Wednesday, Dec. 4; (2) color television schedule of surgical demonstrations emanating from Lankenau Hospital; (3) motion picture program daily plus a special session Tuesday evening, Dec. 3; (4) exhibits featuring a well-

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rounded program and special displays on the history of medicine in the Philadelphia area, and fractures and manikin demonstrations on problems of delivery; (5) panel discussions on cardiovascular disease, cancer, emotional problems of menopause, hypertension, diabetes, arthritis, traumatic injuries; and (6) the General Practitioner of the Year Award to be presented by the A. M. A. to an outstanding family doctor.

TASK FORCE ON HOSPITALIZATION OF THE AGED

During the last week in August two bills were introduced into Congress concerning hospitalization of the aged to be financed by Social Security funds. Realizing the effect of this type of legislation on the practice of medicine, the Executive Committee of the Board of Trustees approved the recommendation of the Committee on Legislation that a task force be appointed to give this issue special attention.

Board Chairman Dr. Edwin S. Hamilton appointed Dr. George M. Fister, Ogden, Utah, chairman of the task force, and designated the following members: Drs. Frank C. Coleman, Des Moines, Iowa; Robert L. Novy, Detroit; George F. Gsell, Wichita, Kan.; and James Duffy Hancock, Louisville, Ky. The Committee will conduct and supervise research designed to gather information relative to the problem of hospitalization of persons over 65 years of age.

The task force will not be called on to prepare or present testimony or engage in legislative activities involved in opposing the pending legislation. These functions will be performed by the Committee on Legislation.

CONGRESS ON INDUSTRIAL HEALTH

The 18th Annual Congress on Industrial Health will be held at the Schroeder Hotel in Milwaukee, Jan. 27 to 29, 1958. The Congress is arranged and sponsored by the Council on Industrial Health of the American Medical Association.

THE AMERICAN PHYSICIAN ON TELEVISION OCTOBER 27

Televiewers will see a composite portrait of the American physician on Sunday, Oct. 27, when "Wide Wide World" will present a program entitled "The House I Enter." The A. M. A. is cooperating with the National Broadcasting Company and the sponsors—General Motors—in the presentation of a 90-minute "spectacular," which will feature "live" pick-ups from Los Angeles; Overbrook, Kan.; Milwaukee; Cleveland; Washington, D. C.; and Atlanta, Ga. Ted Rogers, producer of "The House I Enter," said that the program will show the many facets of medical practice and give the general public an insight into the everyday life of a physician. "Wide Wide World" is seen each Sunday from 4 to 5:30 p.m. (EDT) on the full NBC television network.

NEW EDITOR FOR TODAY'S HEALTH

James M. Liston, Des Moines, Iowa, special features editor for *Better Homes and Gardens*, who has been appointed chief editor of *Today's Health*, will take over his new duties on Nov. 15, relieving Dr. W. W. Bauer of the part-time editorial duties which he has performed for eight years in addition to his responsibilities as Director of the A. M. A. Bureau of Health Education.

Mr. Liston, who is 41, married, and the father of two daughters, took his first editorial job with Rotary International, after teaching high school in Chicago for two years. Later, he was a free-lance radio script writer and a publicity writer for two industrial companies before joining *Better Homes and Gardens* in 1948. He has also written many special features on health subjects.

MEDICAL CIVIL DEFENSE CONFERENCE

The A. M. A. Council on National Defense will sponsor the eighth Annual County Medical Societies Civil Defense Conference on Nov. 9-10, 1957, in Chicago at the Morrison Hotel. These conferences are designed to help local medical and health personnel plan for their roles in disaster and civil defense emergencies.

Congresswoman Martha W. Griffiths of Michigan will report on the status of national civil defense legislation which, in the first session of the 85th Congress, received a considerable amount of attention. Mrs. Griffiths is a member of the House Committee on Government Operations and its Subcommittee on Military Operations.

Another highlight of the conference involves reports on the experience gained through several test operational exercises which were conducted under simulated disaster conditions including a critique of the national exercise "Operation Alert."

There is a lesson to be learned from every disaster. Medical preparedness plans prevented a much greater loss of life last June when Hurricane Audrey struck Cameron and Calcasieu Parishes in Louisiana. Physicians, nurses, and other health personnel were organized and prepared to provide emergency medical and health care. Their response was prompt when the disaster struck. Their work was effective and they proved both the necessity and efficiency of prudent and well-planned disaster organization and preparedness. The program features a one-hour roundup report of operations and experiences gained in the disaster "Hurricane Audrey, 1957." Dr. Joseph A. Hertell will report on general plans and organization in the disaster area, followed by a report on the

activities of hospitals during the disaster from Mr. Joseph W. Hinsley. The experiences of physicians and the role of the local medical society will be discussed by Dr. Leonard K. Knapp.

Individuals desiring additional information on the conference are requested to contact Mr. Frank W. Barton, Secretary, Council on National Defense, American Medical Association, 535 N. Dearborn St., Chicago 10.

PROGRAM
SATURDAY—NOV. 9, 1957
MORRISON HOTEL—COTILLION ROOM

8:00- 9:00 **Registration**

9:00- 9:10 **Call to Order**
James H. Lade, M.D., Director, Office of Medical Defense, New York State Department of the Health, Albany, N. Y.

9:10- 9:15 **Welcome Remarks**
Mr. Frank W. Barton, Secretary, Council on National Defense, A. M. A.

9:15- 9:45 **Future Role of FCDA**
Mr. Lewis E. Berry Jr., Deputy Administrator, Federal Civil Defense Administration, Washington, D. C.

9:45-10:15 **FCDA Health Services Activities**
M. M. Van Sandt, M.D., Director, Health Office, Federal Civil Defense Administration, Battle Creek, Mich.

10:15-10:45 **Exercise Operation Rebound**
Stanley W. Olson, M.D., Dean, Baylor University College of Medicine, Houston, Texas.

10:45-11:15 **Civil Defense in Canada**
Gordon E. Fryer, M.D., Medical Consultant, Civil Defense Health Services, Department of National Health and Welfare, Ottawa, Canada.

11:15-12:00 **Status of National Civil Defense Legislation**
Honorable Martha W. Griffiths, U. S. Congresswoman, 17th District of Michigan.

12:00- 2:00 **Luncheon—Embassy Room—Mezzanine Floor**

2:00- 2:30 **National Damage Assessment Program and Critique of Operation Alert 1957**
Mr. H. Burke Horton, Director, National Damage Assessment Program, Office of Defense Mobilization, Washington, D. C.

2:30- 3:00 **Emergency Care of Head Injuries**
Charles E. Dowman, M.D., Member, Committee on Civil Defense, Medical Association of Georgia, Atlanta, Ga.

3:00- 3:30 **Report on Operation Firedrill—Brooke Army Hospital**
Col. Roland K. Charles, M. C., U. S. Army, Deputy Commander, Brooke Army Hospital, Fort Sam Houston, Texas.

3:30- 5:30 **Workshop Session**
Conferees to be divided into four groups to consider problems and recommended courses of action in following emergency situations:

I—Small localized disaster (100 casualties or less from train wreck, plant fire, collapsed building, etc.; well localized situation with fixed installations intact and medical teams available). Group Leader—J. G. Fred Hiss, M.D., Chairman, Committee on Emergency Medical Service and Civil Defense, Medical Society of the State of New York, Syracuse, N. Y.

II—Natural disaster (over 100 casualties from flood, hurricane, tornado, large fires, etc.; involves large area with fixed installations which may be intact or destroyed or distant from scene of casualties). Group Leader—Mr. John N. Hatfield II, Secretary, Committee on Disaster Planning, American Hospital Association, Washington, D. C.

III—Epidemic disaster, including bacterial or chemical attack hazards. Group Leader—Alexander D. Langmuir, M.D., Chief, Epidemiology Branch, Communicable Disease Center, U. S. Public Health Service, Atlanta, Ga.

IV—Large-scale disaster involving radiation hazards (reactor plant explosion, sabotage, or enemy attack). Group Leader—Paul S. Parrino, M.D., Director, Medical Care Division, Federal Civil Defense Administration, Battle Creek, Mich.

6:15- 7:15 **Social—Suite 440**

SUNDAY—NOV. 10, 1957

9:00- 9:30 **Civil Defense Motivation**
Cortez F. Enloe Jr., M.D., Member, Committee on Civil Defense, Council on National Defense, A. M. A., New York City.

9:30-10:30 **Report of Workshop Sessions**
Dr. Hiss, Presiding.
Group I—Dr. Hiss
Group II—Mr. Hatfield
Group III—Dr. Langmuir
Group IV—Dr. Parrino

10:30-11:00 **A. M. A. Program on Asian Influenza**
Harold C. Lueth, M.D., Chairman, Committee on Civil Defense, Council on National Defense, A. M. A., Evanston, Ill.

11:00-11:30 **A. M. A.—FCDA Study Project Report**
Earle Standlee, M.D., Staff Director, Special A. M. A.—FCDA Study Project, A. M. A.

11:30-12:30 **Selected Film Screening**
"Treatment of Nerve Gas Casualties"
"Operation Pill Hill"

12:30- 2:00 **Luncheon—Embassy Room—Mezzanine Floor**

2:00- 2:30 **Radiological Aspects of Radiation Fall-out—Current Concepts**
Crawford F. Sams, M.D., Medical Officer, FCDA Radiological Study Project Civil, University of California, Berkeley.

2:30- 3:30 **Hurricane Audrey 1957**
General Preparedness Planning
Joseph A. Hertell, M.D., Area Medical Officer, Director, Blood Program, Southeastern Area, American National Red Cross, Atlanta, Ga.
Hospital Operational Preparedness
Mr. Joseph W. Hinsley, Administrator, Lake Charles Memorial Hospital, Lake Charles, La.
Role of County Medical Society
Leonard K. Knapp, M.D., President, Calcasieu Parish Medical Society, Lake Charles, La.

3:30- 4:00 **Business Session—Adjournment**
Dr. Lade, Presiding.

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COUNCIL ON MEDICAL SERVICE

This is the ninth of a series of papers on various aspects of aging. Each paper has been prepared for the Committee on Aging by an authority in the field. When completed, the series will be published in booklet form.

POSTURE IN THE AGING AND AGED BODY

Joseph T. Freeman, M.D., Philadelphia

"Animals have shapes and forms. Only man has posture . . ." [1] The routinely renewed achievement of the complex mechanisms of the upright posture affirms the substantial quality of this human adaptation. This evolutionary accomplishment attracted a roster of students whose observations parallel the most advanced thinking of the past three centuries. A review of these well-documented facts would serve, without novelty, only to refresh memory. The many details limited specifically to the effects of aging on posture, however, are quite a bit less a part of the common knowledge. Postural modifications in the aging body consist of a combination of changes that must occur in harmony. There are anatomic alterations in the skeleton to which the organs of the modified cavities must make accommodation. Adjustments in such contours and parenchymal contents exact a balance in physiological activities. These morphologic and reactive changes are reflected in appropriate biochemical tolerances and blood and tissue levels in the establishment of an effective equilibrium for survival. The tripartite progression must operate in a way that contributes to the older individual's functional adequacy.

The association between the nature of a structure and the character of its activities was recognized by Keith,[2] whose conclusion was an historical culmination of the fact that form probably is a result of its functions. This is not the sort of thought that does much rousing anymore, but it affirmed theories of development that had long been in formulation. Progress from prone to orthograde and finally to a plantigrade status required multiples of changes. A superior method of survival based on the two-footed stance involved compromises in organ size and relationships which had to be threshed out in cycles of evolution. Pulmonary organs, for example, had to be coupled with a thoracic configuration compatible with the upright state. Cerebral blood flow is determined, among other things, by intravascular pressure; the effect of blood carbon dioxide concentration on cerebrovascular resistance; and reflex effects of the fluctuating intracarotid pressures on these vessels.[3] The position of the head, whose shape is a result, in part, of such forces, affects these forces.

Persistence of well-being and length of survival are determined by the ability of organs to adjust with accumulative age. Adequate functions cannot be maintained if there is a break in the continuous liaison of the organs that mediate them. This is as true in a single life cycle as in the phylogeny of the species. Just as these chest and skull and other systems evolved in the many aspects of erect man, lesser adaptations for such changes as aging in the individual's life had to be perfected. The form, to repeat, follows all of the elements of its function.

Structural Changes and Aging

"A number of structural changes are invariable accompaniments of aging." [4] Posture is determined by the total lineaments of the vertebral column. The configuration of curves from skull to coccyx is the quotient of many apposing forces. During maturation there is a balanced series of conformations to the erect state that is followed by piecemeal deterioration in average senescence. Early changes due to age are degeneration of the intervertebral disk and modifications in the apophysial joints; these changes can occur at a variable rate in different components of these structures from individual to individual. One result is a reduction in total columnar resiliency and of the ability of counterpoised muscle groups to maintain accustomed alignment, as gravity is resisted less effectively by the frame of an older person. Although many aging and aged people maintain satisfactory posture, asymmetrical and prior wearing of the anterior arc of intervertebral separation generally results in the accentuation of curves and osteoblastic proliferation at points of contact. Such degenerative bone disease and osteophytosis in sites of unusual ligamentous strain may deter the rate of loss of the basic vertebral contour. It is quite likely that "spondylosis is the commonest disease to which the vertebral column of man is subject . . . as a physiological response to chronic mechanical stimuli." [5]

Clinical Assistant Professor of Medicine, Woman's Medical College of Pennsylvania, and member of the Commission on Geriatrics, Pennsylvania State Medical Society.

Members of the Committee on Aging are Drs. H. B. Mulholland, Chairman, Charlottesville, Va.; Edward L. Bortz, Philadelphia; Henry A. Holle, Austin, Texas; Wingate M. Johnson, Winston-Salem, N. C.; Theodore G. Klumpp, New York; Frederick C. Swartz, Lansing, Mich.; and Cecil Wittson, Omaha. Committee Staff: Mr. George W. Cooley, Secretary, and Mr. Herbert B. Norton, Research Assistant.

From the unmarred, undiseased state of the nontraumatized healthy young person in the fulness of his postural heredity, a host of changes emerge in "natural" aging. There is increased curving of the cervical region compensated by the counterbalancing head.[6] The thoracic bow is increased, with the convexity to the dorsum, while the lumbosacral section tends to a reverse change of direction. The sacrococcygeal articulation becomes more acute as many strains are brought to a focus in this union of the two sets of bones where there is balanced "a bulky superstructure on a small base." In general, elastic tissue properties seem to undergo the initial impairment followed by bone changes, the density or atrophy of which is related to degrees of use and abuse. The sternal bones, meanwhile, fuse into one, held at a greater distance from the dorsal column by the tendency of horizontally rotated ribs to maintain a fixed inspiratory position. As points of muscle origin and insertion, as well as functions, shift, muscles are molded into new shapes as more effective adaptations to gravity. The loss of tone of abdominal muscles unsupported by more rigid means inclines the region to a gravid sag which promotes accumulative defects. The pelvis, as a structure of support and balance, is compressed vertically and expanded laterally. The relationship of the femoral head to the enshallowed acetubulum becomes more acute. The short step, bent knee, and shifted center of gravity of the very old, often cane-supported, person is in contrast to the epitome of successful adaptation, the peak of which was passed in late maturity—"in a better understanding of the special structure and the special physiology of the individual . . . the solution of the problem of chronic disease is largely to be found." [4]

The extensor muscle mass of the flexed cervical-occipital region becomes heavier in contrast to the opposed anterior muscles, which become shorter, atrophic, and spastic. Impaired foraminal apertures and the new lines of muscular emphasis compress segmental nerves with the production of various uncomfortable radicular syndromes. There are vascular, musculoligamentous, as well as neurological effects related to the arthritic articulations.[7] The restricted mobility of the cervical component of the mediastinal structures renders it less reliable as a diagnostic index of intrathoracic changes. Impairment of ability to extend the neck limits coughing, swallowing, and other essential movements which are dependent on an expansible portal to the thorax.

In the deepened and widened and less mobile chest, the lungs are emphysematous in an increasing number of instances with a reduction in the total functional units. The intrathoracic structures of the mediastinum are more fixed. As the more rigid chest approaches a position of inspiratory fixation, accessory respiratory muscles become more essential for primary respiratory function as well as the maintenance of negative intrapleural pressure by which the circuit of venus flow against gravity is established. Infradiaphragmatic veins lengthen, become more tortuous, and undergo degenerative changes with calcific deposition. The time for blood return to the vena cava inferior is prolonged.

The diaphragmatic concavity changes and it undergoes orificial impairments as its modified attachments and prime muscle qualities change. There is an age-linked increased incidence of herniations through the esophageal hiatus which has decreased resistance to repeated strains transmitted from above and below.[8] The postural change of kyphosis may be the point of departure for a pathological sequence of such a hernia and chronic hypochromic anemia. In the area where the gastric mucosa is constricted by the annular esophageal opening and irritated refluxly, there is a varying degree of mucosal extravasation of blood for which there is inadequate compensation to maintain a normal blood level with chronic depletion of iron stores.[9]

The accentuated lumbosacral line is reflected in the impaired muscle qualities of the anterior abdominal wall with its droop of poorly resisted intra-abdominal contents and the accumulations of fat in the various planes and the omentum as well as in the retroperitoneal depots. All types of herniations increase, while fluid retention is linked to the hindered venous return which may effect an expansion of the lower body's total extracellular space. The influence of the modified postural dynamics, among other effects, accounts for a more than coincidental increase in the incidence of intestinal diverticuli, hemorrhoids, and varicosities of the extremities.[10]

The less stable upright state is accompanied by essential changes in the organs of support and locomotion. Degrees of joint deformities from hips to arches, neurological changes, and the progression of peripheral arteriosclerotic states belong in the same parcel. The entire picture, from an occasional aching back to the pathetic *marche a petit pas*, is framed by age's structural deterioration. Osteoporosis goes hand in hand with the obvious articulatory changes. "This machinery is constituted, not on an anatomical, but on a physiological basis." [2]

Biochemical Changes and Aging

As cause or result, biochemical changes must be involved in the structural modifications. Prominent among these are the interrelations of carbon dioxide retention, water balance, and calcium shifts. It might be theorized that localized changes in carbon dioxide concentration due to structural and activity limitations with age are primary. As venous return is impaired by reduced muscle tone, forced or spontaneous reduction in activities, altered pulmonary negative pressure, as well as a complex of other bearings, there is a tendency for dependent parts to be exposed to a lower pH for longer periods of time than nondependent areas. Such zonal differences are, in effect, regions of relative acidosis sub-

ject to constant forces of equalization. Water retention apparent as edema is due not only to the back pressures of gravity and osmotic forces but also to higher concentrations of carbon dioxide.[11] Chronic vasodilatation with sensations of burning, restless legs, and an increased incidence of nocturnal leg cramps may be part of this pattern. Acidosis is associated with increased calcium excretion, and intraosseous as well as extraosseous structures would be subject to regional differences in pH. For simple mechanical reasons or in the many chemical changes subsequent to release from continued dependency (of which adjustment to the carbon dioxide levels is an important consideration) certain muscle groups may become sensitized and respond with tetanic reactions.[12] In fact, the entire problem of calcium metabolism as part of the many influences of postural changes with age could be subjected to survey. Clinically, it is a common observation that the lower tibia, particularly in older women but also in many men, is very sensitive to pressure. This is a region which, by position, is articularly susceptible to many bone-altering effects, of which higher carbon dioxide levels may be thought to be one.

Changes in posture and muscle tone with dilating vascular effects underlie less labile fluxes in blood volume, which are reduced 15% normally by standing for 30 minutes.[13] In older persons, shifts in blood volume, dilated vascular tree, and reduced vessel elasticity are reflected in the increased incidence of recumbent angina, pulmonary edema, acute paroxysmal nocturnal dyspnea, and the motor agitative features of cerebral anoxia. The last are interpreted too often as primary cerebral impairment when a temporary physiological inadequacy unmasks for the time a generally compensated state of chronic brain syndrome.

There are many other influences in addition to these that are operating in such abnormal conditions. Proteinuria[14] is significantly increased in persons in the upright position, and there is a still higher incidence in the lordotic state. Diastolic pressure rises when a person stands, and it falls with recumbency. In the presence of kyphosis[15] there is a reduction in alveolar ventilation, reduced arterial oxygen tension, increased pulmonary vascular pressure, and a tendency to a rise in pulmonary vascular pressure. Vital capacity and maximum breathing capacity are reduced in direct relation to age. Circulation time increases and venous pressures tend to be higher. Such changes affect and are influenced also by shifts in electrolytes. In brief, as Sodeman stated, "the mechanisms of homeostasis have physiologic limitations."

Obviously no single influence, such as postural change, can be blamed for the innumerable adjustments undergone in the aging body whose concert of successful and complicated progressions must be made in synchrony. The danger, by far, is not that too much will be ascribed hypothetically to structural balances but that too little will be accepted as related to all that is involved in such efforts in a life cycle.

Comment

Is there any evidence of correlation in good posture, well-being, the incidence of certain pathological conditions, and length of survival? Clinical impressions suggest an affirmative answer. Better postured individuals probably have fewer defects, enjoy better health, and live longer than those with a seriously distorted skeleton. Postural aging is attended by new anatomic zonings and accommodating physiological states which can attain a pathological status reflected in new blood and tissue chemical constants. The extensive range of variable change only suggested in this arbitrarily limited synthesis depends on the degree of physical deformity and inherent abilities to make balanced adjustments. Lesser changes would incite lesser degrees of reaction and have a reduced influence on tenure. With the rise in postural impairments, there is a curtailment of resistance to physical and chemical stresses. One familiar example is the pattern of kyphoscoliotic cardiopulmonary disease in which the use of morphine, for example, may have undue effects. This vascular limitation based on a gross thoracic change is an extreme form, lesser stages of which have proportional effects.

In linking body limitations to structural deficiencies, there emerges the awareness of the need to promote techniques that will be more effective in resisting average trends of aging. If the morphologic, physiological, and biochemical changes based hypothetically on structure alterations can be allied inextricably to body form and function, a single question emerges, namely, will a conscious and persistent effort to maintain good posture in the face of common senescent regressions be able to impede any or all of the implied consequences? Occasional long survival despite severe architectural aberrations indicates a capacity of the body to arrive at a working premise, but this is rare. In general, there is a correlation in body structure, health, and span of survival.

As a pragmatic as well as a therapeutic feature in medical care, there are considerations that would best be undertaken prophylactically at an age before inalterable geriatric changes occur and yet be useful after the occurrence of some degree of them. These are (1) the promotion of the best postural state compatible with the body's older capacities and (2) the utilization of purposeful activities, correct nutrition, anabolic supplementation, and training in correct body alignment as a counterpart to natural adaptations made by the aging and aged body in its own defense. An over-diligent effort to correct posture in the face of a certain established equilibrium might seem justified empirically but may be unsound physiologically, particularly if

forced and in haste. Postural treatment must be planned with deliberation for the long pull and must be allied to normal values in gerontology, with consideration for the following statement made by Nascher a half-century ago: "in dealing with senile disease the object must be to restore the organism to the normal senile state and not to the normal state of maturity." The result will be an effective survival based on better anatomic and physiological conformity to the serial stages of aging.

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BUREAU OF MEDICAL ECONOMIC RESEARCH

There is presented below a summary of bulletin 104, "Accident Burden on Hospitals," a detailed survey of the burden of inpatients in the accident category on American hospitals, the attending physicians, hospital personnel, and facilities. This is the third in the series of bulletins designed to estimate the totality of services rendered annually by American physicians to their patients. The two earlier bulletins in this series were number 97, "Age and Sex Distribution of Hospital Patients," and number 102 and 102A, "Some Categories of Patients Treated by Physicians in Hospitals." A copy of each of these three bulletins may be obtained by writing to the Bureau of Medical Economic Research, American Medical Association, 535 N. Dearborn St., Chicago 10, Ill. Bulletin 104 (Dickinson and Martin) will be available about Dec. 1.

FRANK G. DICKINSON, PH.D., *Director.*

ACCIDENT BURDEN ON HOSPITALS

What is the burden imposed upon American hospitals and, more particularly, upon physicians by the steady stream of patients injured in accidents? What proportion of patients discharged, particularly from the general and special hospitals, were in the accident category? What proportion of the total patient-days were accounted for by persons hospitalized for accidents? How many millions of dollars were expended by hospitals during the year to take care of these accident cases? The results of our search for answers to these and related questions are presented in bulletin 104 and in the summary below.

This study, as its title indicates, was confined to hospitals and to the classification of accidents as defined by references to Standard Nomenclature of Diseases and Operations, fourth edition. The data were collected originally for the month of November, 1955. Data were also obtained for March, 1956, for many of the hospitals that did not respond to the original request. The role of accidents in mental and tuberculosis hospitals was so minor that the data in this summary refer only to our estimates for the 6,000 general and special hospitals.

The data for patients discharged during November, 1955, indicate the following findings:

1. The 128,000 inpatients discharged who were hospitalized because of accidents comprised 6.9% of all patients discharged during the month.

2. The total inpatient-days for these inpatients were 1,370,000, or 8.1% of total inpatient-days for

all inpatients discharged during the month; the average length of stay was longer—10.7 days versus 9.1 days—for accident inpatients.

3. Of the total inpatients discharged during the month who were hospitalized because of accidents, 65.2% were males—11.3% under 15 years of age, 35.6% in the age group 15-44, 13.1% in the age group 45-64, and 5.2%, 65 years and over; and 34.8% were females—5.8% under 15 years of age, 12.4% in the age group 15-44, 8.6% in the age group 45-64, and 8.0%, 65 years and over.

4. Although our term "emergency room" was subject to some misinterpretation, 31.8% of all patients (outpatients and inpatients) seen in emergency rooms were accounted for by accidents.

5. During the reporting year (ending Sept. 30, 1955, for most hospitals) the care of accident patients required expenditures of 311 million dollars, or 7.4% of the total annual expenses of the 6,000 general and special hospitals. (Presumably the total for 1957 involved many more millions of dollars.)

6. The annual payroll expense of these hospitals for the treatment of accident cases was 198 million dollars, or 7.3% of the total payroll.

7. The personnel devoted to the care of accident cases totaled 68,200, or 6.7% of total personnel.

8. The accident cases required the use of 50,500 beds, or 6.7% of the total beds.

Depending upon the criteria used in the measurements, we conclude that the treatment of accident cases accounted for 7 to 8% (6.7 to 8.1%) of the burden on the general and special hospitals of the United States. Presumably the burden on physicians came within the same range. The burden of accident cases treated by physicians in the home and in the office will be estimated in a later bulletin in this series.

This and other studies in the series could not have been made without the splendid cooperation of the medical staffs, the administrators, and the medical record librarians of the responding hospitals. Since our previous studies have shown that the burden of another nondisease category, pregnancy, is approximately 18% of one total, we conclude that the treatment of disease in general and special hospitals of the United States is roughly three-fourths of the total burden.

MEDICINE AND THE LAW

Hospital Records: Limitations on Admissibility.—This was an action for damages for injuries resulting from the alleged malpractice of the defendant physician. From a judgment in favor of the plaintiff, the physician appealed to the Supreme Court of Washington.

It appears from the report of this case that the plaintiff contended that the defendant physician failed properly to diagnose and subsequently treat a child's illness so that the child suffered from encephalitis following diphtheria. In order to establish her claim, the plaintiff offered in evidence a hospital record made about two years after the alleged injury and at a time when the child was taken to a hospital for treatment for epilepsy by a doctor other than the defendant. The present malpractice suit had already been filed. The principle issue involved in this case was as to the admissibility of the hospital record.

The plaintiff contended that the record was admissible under the uniform business records act which provided: "A record of an act, condition, or event, shall insofar as relevant, be competent evidence if the custodian or other qualified witness testifies to its identity and the mode of its preparation, and if it was made in the regular course of business, at or near the time of the act, condition or event, and if, in the opinion of the court, the sources of information, method and time of preparation were such as to justify its admission." Objected to most seriously was that portion of the record containing "Diagnosis: Convulsive disorder secondary to residuals of encephalitis following diphtheria."

A business record, said the Supreme Court of Washington, is admissible only insofar as it represents a record of a contemporaneous act, condition, or event. The uniform business records act, as applied to this case, admits the record as evidence of the following: (1) the event (the fact that the child was brought to the doctor because of illness), (2) the condition (the doctor's present determination that the child was suffering from epilepsy), and (3) the act (the doctor's treatment of the illness). A diagnosis of epilepsy is a relevant part of the business record. However, a determination that the epilepsy was the result of diphtheria is a conclusion based upon speculation and conjecture, and does not constitute an "act, condition, or event," within the purview of this statute. We hold that a medical opinion as to causation, which is not the result of an observed act, condition, or event, cannot be established by a business record.

In view of the fact that the record had been admitted by the trial court, the judgment of the trial court in favor of the plaintiff was reversed and a new trial ordered. *Young v. Liddington, 309 P(2) 761 (Washington, 1957).*

MEDICAL NEWS

ALABAMA

Name Chairman of Department of Medicine.—Dr. Walter B. Frommeyer Jr. has been appointed chairman of the department of medicine of the Medical College of Alabama, Birmingham, succeeding Dr. Tinsley R. Harrison, who will continue as professor in the department. Dr. Frommeyer became assistant dean in July, 1954. For three years, he was assistant professor of medicine at the Medical College and director of the blood bank and tumor clinic at University Hospital, and formerly, was a research fellow at the Thorndike Memorial Laboratory, Harvard University Medical School, Boston, for one year.

Personal.—Dr. William G. Thuss Jr. has been appointed the first associate professor of industrial medicine in the department of preventive medicine and public health, Medical College of Alabama, Birmingham. A native of Birmingham, Dr. Thuss received the doctor of science degree in industrial medicine from the University of Cincinnati in 1956. He is also medical director of Hayes Aircraft Corporation.

DISTRICT OF COLUMBIA

Diagnostic Building at Georgetown University.—Construction began Sept. 16 on the new Gorman Diagnostic Building in the Georgetown University Medical Center. The 3-million-dollar structure will stand at the rear of the present hospital building. The building is named to honor the late Rev. Lawrence C. Gorman, S. J., Georgetown president from 1942 to 1949. The new structure will house diagnostic, outpatient, and research facilities and will free space in the existing hospital to provide 40 additional rooms for patients. The exterior walls will be of brick, limestone, and glass in a design which will be followed in all future buildings in the center. Funds for the building came from several sources, including the Ford Foundation, the Geschicketer Foundation, and federal grants.

GEORGIA

Appoint Chairman of Pediatrics Department.—Dr. Victor C. Vaughan III has been appointed chairman, department of pediatrics, Medical College of Georgia, Augusta. Dr. Vaughan has served as assistant resident, New Haven Hospital of Yale University, New Haven, Conn.; research fellow, Harvard Medical School, Boston; assistant professor, Yale University School of Medicine, and associate professor of pediatrics, Temple University School of Medicine, Philadelphia. He is a member of the American Academy of Pediatrics, the Society for Pediatric Research, Philadelphia Pediatric Society, the American Society of Human Genetics, and the American Federation for Clinical Research, and a diplomate of the American Board of Pediatrics.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

ILLINOIS

Personal.—Dr. Ruth E. Church has been appointed deputy director in charge of the Division of Hospitals and Chronic Illness of the Illinois State Department of Public Health. She succeeds Dr. G. Howard Gowen who resigned to accept a position with the International Cooperation Administration in Santiago, Chile.——Dr. Elvin L. Sederlin, Helena, Mont., has been appointed director of the Adams County Department of Health, succeeding Dr. Harry O. Collins, who resigned in 1956, following 25 years of service.

Chicago

Medical Film Wins International Awards.—Dr. Hans von Leden and Paul Moore, Ph.D., Northwestern University Medical School, have received two international awards based on a motion picture, "The Function of the Normal Larynx." The first award, the Minerva, was presented at the International Film Festival for Medical and Scientific Films, Turin, Italy. The second award, a silver robot, was presented at the III International Congress for Specialized Cinematography, Rome, Italy, for the perfection of a new technique in recording laryngeal function by high-speed photography. The motion picture portrays a new method of studying laryngeal functions.

IOWA

Personal.—Dr. James F. Speers has been appointed director of the Des Moines Health Department. Dr. Speers practiced for three years in Titusville, Fla. He holds a master of public health degree from the Medical College of South Carolina.

Dr. Peterson Honored.—Dr. Frank R. Peterson, of Cedar Rapids, has been honored as recipient of the 1957 distinguished service award, given by the Mississippi Valley Medical Society. Dr. Peterson, past-president of the society, was formerly head,

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department of surgery, State University of Iowa's College of Medicine, Iowa City, and is president of the Iowa State Board of Examiners.

MASSACHUSETTS

Cutter Lecture in Boston.—Dr. Charles M. Fletcher, senior lecturer in medicine, Postgraduate Medical School of London, and formerly director of the Medical Research Council's Pneumoconiosis Research Unit, will deliver the Cutter Lecture on preventive medicine Oct. 29 at 5 p. m. in Amphitheater D, Harvard Medical School, Boston. Dr. Fletcher will speak on the "Epidemiology of Chronic Disabling Respiratory Disease."

MICHIGAN

Personal.—Dr. Osborne A. Brines, professor of pathology, Wayne State University Medical School, Detroit, was elected president of the International Society of Clinical Pathology at its triennial session in Brussels, recently. The society, founded 10 years ago, is made up of constituent societies from 23 countries. Dr. Brines, past-president of the American Society of Clinical Pathologists, was vice-president of the international group from 1949 until his election to the three-year presidency last July. The next meeting of the society will be held in Madrid in 1960.

MICHIGAN

University Grants.—More than a million dollars in gifts and grants to Wayne State University recently was accepted by the university's Board of Governors. Largest single grant was $500,000 from the National Institutes of Health, an agency of the U. S. Public Health Service. When matched by funds from the university, the grant will be used for construction of a "Life Science Research Center." A $425,000 grant came from the estate of the late Richard Cohn, Detroit advertising and publishing executive. The endowment will be used toward the construction of a new College of Nursing and Graduate School building which will bear Mr. Cohn's name. Other gifts and grants in research, educational programs and student-aid funds totaled $366,300. A major portion of $225,994 went to medical research and training programs. Included was a grant from the Michigan Heart Association of $44,677 to be used in continuing eight research projects. The Rands Family Foundation gave $10,000 to continue research fellowships in the field of geriatrics.

MONTANA

State Medical Election.—At the annual meeting of the Montana Medical Association the following officers were elected: president, Dr. John A. Layne, Great Falls; president-elect, Dr. Herbert T. Caraway, Billings; vice-president, Dr. Leonard W. Brewer, Missoula; secretary-treasurer, Dr. Theodore R. Vye, 412 North Broadway, Billings, Mont.; and assistant secretary-treasurer, Dr. William E. Harris, Livingston. The next annual meeting of this association will be in Billings, Sept. 11-13, 1958.

NEBRASKA

Personal.—Dr. Henry J. Lehnhoff Jr., Omaha, has been named medical director of Woodmen of the World Life Insurance Society. The appointment fills the vacancy created by the death of Dr. Herbert B. Kennedy, who held the post for 22 years. Dr. Lehnhoff is senior member of the staffs of Clarkson and Methodist hospitals and is also a member of the staffs of Lutheran and Immanuel hospitals.—Dr. Archibald R. McIntyre, chairman, department of physiology and pharmacology, University of Nebraska College of Medicine, Omaha, has returned from a summer trip up the Amazon River of South America. Dr. McIntyre attended the first International Symposium on Curare at Rio de Janeiro at the invitation of the Brazilian government and UNESCO.

NEW YORK

Reiss Memorial Lecture.—The New York Institute of Clinical Oral Pathology announces the sixth Herman L. Reiss Memorial Lecture to be held at the New York Academy of Medicine Building Oct. 28, 8:30 p. m. The essayist will be Dr. Iago Galdston, secretary, Medical Information Bureau, New York Academy of Medicine, who will lecture on, "The Birth and Death of Specialties." Members of the medical, dental, and allied professions are invited.

Personal.—Dr. George W. Dana has been appointed director of the North Shore Hospital, Manhasset, replacing John M. Danielson, who resigned to become administrator at the Evanston Hospital, Evanston, Ill. He is presently medical director of the Bingham Associates Fund in Boston and is also medical staff director of the New England Center Hospital, assistant professor of medicine, Tufts University School of Medicine, and a member of the faculty of Harvard University.

General Practice Meeting.—The ninth annual scientific assembly of the New York State Academy of General Practice will be held Oct. 21-23 at the Barbizon-Plaza Hotel, New York City. George R. Metcalf, New York State senator, 48th district, will present "Economic Safeguards Over 65," Oct. 22. The program includes the following topics: atomic medicine, geriatric problems, dislocations and fractures (closed-circuit TV program), newer chemotherapeutic aids in nervous and mental disorders, and obstetrical program for the GP. The following topics by out-of-state speakers are scheduled:

Applications of Atomic Medicine in Modern Diagnosis, Dr. George V. Taplin, director of atomic medicine research, University of California at Los Angeles Medical School.

The Role of the GP in Radioisotope Therapy, Dr. George Meneely, president, American College of Cardiology.

Psychological Aspects of the Aging, Dr. William Malamud, professor of psychiatry, Boston University.

Tremor in the Aging—Symptom or Disease, Dr. Albert England, assistant in urology, Harvard Medical School, Boston.

The Mood Disorders, Dr. Francis J. Braceland, president, American Psychiatric Association.

The Schizoid and Schizophrenic Disorders, Dr. Raymond W. Waggoner, director, Neuro-Psychiatric Institute, University of Michigan Medical School, Ann Arbor.

Special topics, rehabilitation medicine and health program in atomic medicine, will be presented Oct. 24. Technical and scientific exhibits are planned, and a ladies' program has been arranged. The banquet will be Oct. 22, 7 p. m. For information write the New York Academy of General Practice, Dr. Raymond S. McKeeby, Secretary-Treasurer, 84 Main St., Binghamton, N. Y.

New York City

Personal.—Dr. Robert B. McGraw has retired as chief of the psychiatric clinic, Vanderbilt Clinic, but will continue as a member of the executive committee of the department. Dr. Robert Senescu was appointed Chief of the Vanderbilt Psychiatric Clinic as of July 1.

Dr. Cecil Receives Award.—Dr. Russell L. Cecil has been honored as recipient of the 1957 honor award, a plaque and gold medal, given by the Mississippi Valley Medical Society. Dr. Cecil is emeritus professor of medicine, Cornell University College of Medicine, and editor of "A Textbook of Medicine." The citation in connection with the award reads in part: "From your laboratory came the streptococcus agglutination test, progenitor of the current serological tests for rheumatoid arthritis; from your vision arose flourishing organizations and from your zeal, the inspiration to young investigators, all dedicated to the conquest of arthritis. In 1926, you made a great contribution to medical education, the first multiple author textbook of medicine in this country."

Grants for Training in Pathology.—The department of pathology, New York University–Bellevue Medical Center, has been awarded about $450,000 for a five-year period to train physicians for research and teaching careers in pathology. The training program, which began July 1, was made possible through a grant from the National Institutes of Health and will be directed by Dr. Lewis Thomas, chairman, department of pathology of the University College of Medicine.

There are eight research fellowships available at the level of assistant resident. The stipend ranges from $3,600 to $4,500 yearly. In addition, two senior fellowships are available for physicians with more advanced training in the basic sciences on anatomical pathology, with a stipend of $7,500 annually. Information may be obtained from the Dean, New York University College of Medicine, 550 First Ave., New York 16, N. Y.

OHIO

Blankenhorn Memorial Fund.—Establishment of a Marion A. Blankenhorn memorial research fund in the University of Cincinnati department of internal medicine was announced by Dr. Walter C. Langsam, president of the university, following memorial services for the distinguished physician-educator, who died Sept. 3. The memorial will be used for pressing research needs of the College of Medicine and for lecturers on research topics. Dr. Stanley E. Dorst, dean of the College of Medicine, and Dr. Richard W. Vilter, Dr. Blankenhorn's successor as head of the department of internal medicine, will be in charge of the fund. Dr. Blankenhorn was head of the department for 22 years, retiring in 1956.

OREGON

Personal.—Dr. Herbert E. Griswold Jr., associate professor at the University of Oregon Medical School has begun a year's leave of absence to study in England and Sweden. His year of study is made possible through a grant from the American Heart Association and support from the Irwin Memorial Fellowship Fund of the Oregon Heart Association. He will go to the Institute of Cardiology of the National Heart Hospital, London.——Dr. James L. Wooden was honored recently when a "day" in his honor was celebrated in recognition of his 50 years of practice in the city of Clatskanie. A series of talks were featured which recalled Dr. Wooden's years of community practice. He began practice in Clatskanie on Aug. 12, 1907. ——Dr. Robert H. Tinker, vice-president and chairman of the education committee, Oregon Chapter, American Academy of General Practice, has accepted a three year appointment to the American Academy of General Practice Commission on Postgraduate Education. Dr. Tinker, who has served for two years as head of Oregon's education committee, is now the northwest regional representative for the national commission.

PENNSYLVANIA

Annual Scientific Day.—The seventh annual scientific day of the Medical Alumni Association of the University of Pittsburgh will be held Nov. 1 at the Mellon Institute in Pittsburgh. The speakers will be Dr. Robert J. Boucek, associate professor of medicine, University of Miami School of Medicine; Dr. Charles F. Wilkinson, professor, department of medicine, New York University School of Medicine; Dr. Charles Dunham, director, division of biology and medicine, Atomic Energy Commission; and Dr. Perry B. Hudson, assistant professor of urology, Columbia University College of Physicians and Surgeons.

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Philadelphia

Dr. Sevy Heads Pharmacology Department.—Dr. Roger W. Sevy has been promoted to head the department of pharmacology at the Temple University School of Medicine, succeeding Dr. Dean A. Collins, now research professor of pharmacology. Dr. Sevy has been a member of the faculty since 1954, when he was appointed assistant professor of pharmacology. Last year, he was promoted to a full professorship. From 1947 to 1948, he was a Life Insurance Medical Research Foundation Fellow at the Vermont College of Medicine.

Laboratory for Cancer Studies.—A grant of $150,000 for the construction and operation of a laboratory for biochemical studies in cancer at Hahnemann Medical College has been awarded Dr. Julius Schultz, associate research professor in biochemistry, by the National Cancer Institute. With $102,000 in operating funds guaranteed for the next five years, another grant of $40,000 for additional operating funds is expected. The investigation into the biochemical aspects of cancer will be aimed at understanding the mechanism of cancer formation and at the rational utilization of chemical compounds to inhibit tumor growth.

SOUTH DAKOTA

Annual District Seminar.—The Huron District Medical Society, Huron, announces the third annual Central South Dakota Medical Seminar to be held Oct. 26-27. The first session will open at 8:30 a. m. Oct. 26, the opening day of pheasant-hunting season, with registration at St. John's Hospital Auditorium. The program includes the following topics and speakers:

Extrophy of the Urinary Bladder, Dr. William G. Schultz, Tucson, Ariz.

Salt and Water Therapy in Pediatrics: the Do's and Don'ts, Dr. Edmund C. Burke, department of pediatrics, Mayo Clinic, Rochester, Minn.

Medico-Legal Medicine, Joseph Koucky, L.L.D., Chicago.

Management of Complications of Acute Nephritis, Dr. Burke.

Registration fee of $10 will include the stag dinner Oct. 27. Credit from the American Academy of General Practice is available. Hunting will be done each afternoon. For information write Dr. Fred Leigh, Chairman, Pheasant Hunting Seminar, Huron Clinic, Fourth Street at Kansas Avenue, Huron, S. D.

TEXAS

Muscular Dystrophy Clinic.—A research project, jointly sponsored by the National Muscular Dystrophy Research Foundation, Inc., and the University of Texas School of Medicine, Galveston, will use $250,000 to establish a Muscular Dystrophy Clinic at the university. Initial studies will be made on two muscular dystrophy patients a week, which later will be expanded to include more patients.

PUERTO RICO

New Medical Center.—The Medical School of the University of Puerto Rico will be relocated on a site with four new hospitals, in each of which it will have teaching and research facilities, when a proposed medical center is completed in San Juan. Toward the costs of a comprehensive study to plan the functions and design of the relocated school, the Rockefeller Foundation has appropriated $75,000 to the university.

The new center, comprising cancer, workmen's compensation, municipal, and district hospitals, together with the medical sciences building of the university, will increase the effectiveness of all five institutions by enabling them to pool their resources and coordinate their services. It will also provide the most densely populated area of Puerto Rico with its first centrally located facility for medical care on a large scale.

The study will deal with the space and other functional requirements of the medical school and especially with its relationship to the four hospitals of the center. It will also include a review by the university medical faculty of its teaching aims, taking into account current trends in medical education and their implications for the future. Probable educational developments over the next 10 to 20 years will be considered in formulating plans and building specifications.

GENERAL

Nominations for Nutrition Awards.—Nominations are invited for the 1958 Borden award in nutrition and the 1958 Osborne and Mendel award for research in nutrition. Nominations may be made by anyone and must be submitted by Jan. 1, 1958, to the chairman of the appropriate nominating committee. Membership in the American Institute of Nutrition is not a requirement for eligibility and there is no limitation as to age. For details write the American Institute of Nutrition, Office of the Secretary, Room 9D 20, Building 10, National Institutes of Health, Bethesda 14, Md.

Air Pollution Conference.—A semi-annual technical conference sponsored by the Air Pollution Control Association will be held Nov. 18-19 at the Fairmont Hotel, San Francisco. Theme for the program is "Particles—Liquid and Solid: Their Role in Air Pollution." Speakers' topics include effects of particulates, sampling and evaluation, types and levels of particulates in contaminated atmospheres, and control at source. About 20 papers are scheduled with panel discussions to follow the formal presentations. Registration fee is $15. For information write the Air Pollution Control Association, 4400 5th Ave., Pittsburgh 13.

Grants for Research in Blindness.—The Scientific Advisory Committee of the National Council to Combat Blindness, Inc., is now accepting applications for "Fight for Sight" grants-in-aid, research fellowships, and summer student fellowships. The committee will consider all applications at its annual meeting in June, 1958. The closing date for receipt of completed applications has been advanced to March 1, 1958. Appropriate forms may be obtained by writing the Secretary, National Council to Combat Blindness, Inc., 41 West 57th St., New York 19, N. Y.

Van Meter Prize Award.—The American Goiter Association again offers the Van Meter Prize award of $300 and two honorable mentions for the best essays submitted concerning original work on problems related to the thyroid gland. The award will be made at the annual meeting of the association, which will be held in the St. Francis Hotel, San Francisco, June 17-19, 1958, providing essays of sufficient merit are presented in competition. The essays may cover either clinical or research investigations, should not exceed 3,000 words in length, and must be presented in English. Duplicate typewritten copies, double spaced, should be sent to the Secretary, Dr. John C. McClintock, 149½ Washington Ave., Albany 10, N. Y., not later than Feb. 1, 1958.

Mental Health Study.—The Joint Commission on Mental Illness and Health has announced receipt of a $60,000 grant from the Rockefeller Brothers Fund to further its three-year survey of the nation's mental health needs and resources. The commission said that it would use this contribution to assist in financing a study of the role of religion in mental health. The study is expected to be finished early in 1959. The commission, made up of representatives from 27 national agencies concerned with mental health, is a nongovernmental agency operating under federal and private grants. It is now in the second year of a multi-faceted analysis and evaluation of the United States' needs and resources for promoting mental health. With headquarters in Cambridge, Mass., it has 12 projects in progress.

Scholarships for Neuromuscular Studies.—The Sister Elizabeth Kenny Foundation has announced a continuance of its postdoctoral scholarships to promote work in the field of neuromuscular diseases. The scholarships are designed for scientists at or near the end of their fellowship training in either basic or clinical fields concerned with the broad problem of neuromuscular disease. Kenny Foundation scholars will be appointed annually. Each grant provides a stipend of from $5,000 to $7,000 a year for a five-year period, depending on the scholar's qualifications. Candidates from medical schools in the United States and Canada are eligible. Inquiries should be sent to Dr. Edgar J. Huenekens, Medical Director, Sister Elizabeth Kenny Foundation, 2400 Foshay Tower, Minneapolis 2, Minn.

Society News.—Newly elected officers of the **Academy of Psychosomatic Medicine** include Dr. Ethan A. Brown, Boston, president; Dr. Lester L. Coleman, New York City, vice-president; Dr. Carlos Seguin, Lima, Peru, second vice-president; Dr. William S. Kroger, Chicago, secretary; and Dr. George F. Sutherland, Baltimore, treasurer.——At a recent meeting of the **Southwestern Society of Nuclear Medicine,** the following officers were elected for the coming year: president, Dr. Jack G. S. Maxfield, Dallas; president-elect, Dr. Herbert C. Allen, Houston; first vice-president, Dr. R. C. Norman, San Antonio; second vice-president, Dr. Samuel B. Nadler, New Orleans; secretary-treasurer, Dr. James R. Maxfield Jr., 311 Medical Arts Building, Dallas 1, Texas.

Foreign Interns and Residents.—More than 6,700 foreign interns and residents for 88 countries around the world trained in American hospitals last year, according to a survey released by the Institute of International Education. Of this group, 4,753 served as residents and 1,988 trained as interns in hospitals throughout the U. S. They were scattered throughout 44 states, the District of Columbia, Hawaii, and Puerto Rico. However, most of them (75%) were concentrated in 10 states, with one-quarter of them in New York State hospitals, and one-half of them in hospitals in Ohio, Illinois, Massachusetts, Pennsylvania, New Jersey, Missouri, Maryland, Michigan, and Texas. The four hospitals with the largest group of foreign interns and physicians were Bellevue in New York City (114), Boston City in Boston (75), Medical Center in Jersey City (75), and Henry Ford in Detroit (66).

Cruise Congress of Ophthalmologists.—The Pan American Association of Ophthalmology, an organization representing all the countries of the Western Hemisphere, will hold its second cruise congress, Feb. 1-14, 1958, on board the S. S. Queen of Bermuda. The itinerary includes a day each in San Juan, Puerto Rico; Ciudad Trujillo, Dominican Republic; Kingston, Jamaica; Port-au-Prince, Haiti; and Nassau, Bahama Islands. Symposiums, free papers, motion pictures, seminars, and exhibits stressing subjects of current interest in diseases of the eye are planned. Meetings will be held on shipboard and also in port cities with local societies of ophthalmologists. There will be opportunities to visit hospitals and to meet the staffs of medical schools in the islands. For information write Mr. Leon V. Arnold, 33 Washington Square West, New York 11, N. Y.

Rehabilitation Fund.—The World Rehabilitation Fund, a voluntary agency, is sponsoring international rehabilitation projects throughout the world. Dr. Howard A. Rusk, New York, is its chairman. One of the fund's early projects is technical assistance in developing rehabilitation services in the Philippines. Two shipments of artificial limbs have already been made to the islands, and the American President Lines has made available funds for a fellowship through which a Philippine physician is enabled to receive advanced training in rehabilitation and physical medicine in the United States. Rehabilitation personnel from other countries have been assisted to study in the United States, books and periodicals have been provided, rehabilitation demonstrations and conferences have been sponsored in various countries, and some artificial limbs have been provided for Thailand.

Symposium on Cancer of Head and Neck.—The American Cancer Society, Inc., will present its annual scientific session at the Park Sheraton Hotel, New York City, Oct. 28-29 with the theme "Cancer of the Head and Neck." Dr. David A. Wood, president of the society, will present an address Oct. 28. Planned discussion topics include: pathological diagnosis of lesions of the oral cavity; problems of anesthesia in surgery of head and neck cancer; and management of lip cancer. Three panel discussions are scheduled: problems in thyroid cancer, moderated by Dr. Thomas J. Anglem, Massachusetts General Hospital; management of cancer of the tongue, moderated by Dr. Danely P. Slaughter, University of Illinois College of Medicine, Chicago; and cancer of the larynx, moderated by Dr. Chevalier L. Jackson Jr., Temple University School of Medicine, Philadelphia. Physicians and members of allied professions are invited. For information write the American Cancer Society, Inc., 521 West 57th St., New York 19.

Prof. A. P. Mathews Dies.—Albert Prescott Mathews, Ph.D., former chairman of the department of physiology at the University of Chicago, died Sept. 21 at a nursing home in Albany, N. Y., aged 85. Dr. Mathews was born in Chicago in 1871. He became an assistant in biology at the Massachusetts Institute of Technology in 1892; assistant professor at Tufts College Medical School, Boston, in 1899; instructor in physiology at Harvard Medical School, Boston, in 1900; assistant professor of physiological chemistry, University of Chicago in 1901, and was chairman of the department of physiology there from 1909 to 1916. He served as captain in the Quartermaster Corps of the Army in World War I, then became professor of biochemistry at the University of Cincinnati, from which position he retired in 1939. For many years, Dr. Mathews was chairman of the physiology department at the Marine Biological Laboratory, Woods Hole, Mass. He was the author of textbooks and numerous articles in scientific journals.

Heart Association Meeting.—The 13th annual scientific session of the American Heart Association, commemorating the tercentenary of William Harvey, will be held Oct. 25-28 at the Hotel Sherman, Chicago. The Lewis A. Conner Memorial Lecture, "Rheumatic Heart Disease—A Challenge," will be presented by Dr. Charles H. Rammelkamp Jr., Cleveland. The George E. Brown Memorial Lecture, "Current Evaluation of the Thrombosis Problem," will be given by Dr. Nelson W. Barker, Rochester, Minn. A symposium on heart sounds and murmurs is scheduled for Oct. 25, with Dr. Victor A. McKusick, Baltimore, as chairman. The program includes the following panel discussions and moderators:

Prevention and Management of Cardiovascular Emergencies, Dr. Howard B. Sprague, Boston.

Unsettled Clinical Questions in the Management of Cardiovascular Disease, Dr. Louis N. Katz, Chicago.

Present Status of Lipid Metabolism and Atherosclerosis, Dr. Herbert Pollack, New York City.

Community Service—Its Nature and Its Significance for Heart Associations, Dr. Ray E. Trussell, New York City.

The annual dinner Oct. 27 will feature Mr. Ralph Edwards as guest of honor. For information write the American Heart Association, 44 E. 23 St., New York 10.

Allergy Meeting in Charleston.—The 12th annual meeting of the Southeastern Allergy Association will be held Nov. 1-2 at the Fort Sumter Hotel, Charleston, S. C. Dr. William B. Sherman, president, American Academy of Allergy, will speak on "Non-Immunologic Factors in Allergic Reactions" and Dr. Orville Withers, president, American College of Allergists, will speak on "The Problem of Food Allergy." The program includes the following topics and speakers:

Cardiac Allergy, Dr. Raymond Arp, Atlanta, Ga.

Allergic Vasculitis, Dr. William A. Thornhill Jr., Charleston, W. Va.

Immunology, Dr. Oscar Swineford Jr., Charlottesville, Va.

Hodgkin's and Allergy, Dr. Jack M. Rose, Houston, Texas.

Mechanisms Concerned with Dysponea in Patients with Pulmonary Disease, Dr. John Guerrant, Charlottesville, Va.

Tranquilizers in Patients with Emphysema, Dr. Oscar Hansen-Pruss, Durham, N. C.

Potassium Iodide Sensitivity, Dr. Lamar Peacock, Atlanta.

Vitamin and Mineral Balance, Dr. Paul Coughlin, Tallahassee, Fla.

Insect Allergy, Dr. Carl Jones, Atlanta.

A clinical-pathological conference is scheduled for the morning of Nov. 2. A cocktail hour and banquet will be held the evening of Nov. 1. For information write the Southeastern Allergy Association, Dr. Katherine B. MacInnis, Secretary-Treasurer, 818 Albion Road, Columbia, S. C.

Meeting of Inhalation Therapists.—The annual meeting of the American Association of Inhalation Therapists will be held Nov. 4-8 at the Hotel Hollenden, Cleveland. Dr. Thomas D. Kinney, president, Cleveland Academy of Medicine, will present an address Nov. 4. The following panel discussions are scheduled: pressure breathing, inhalation therapy in catastrophe, oxygen tent therapy, and organizing and maintaining an inhalation therapy department. The program includes the following luncheon speakers and subjects:

Inhalation Therapy and the Practice of Medicine, Dr. Henry A. Zimmerman, director, Coakley Cardiovascular Laboratory, St. Vincent's Charity Hospital, Cleveland.

Civil Defense Training and Coordination for Inhalation Therapists, Dr. Paul S. Parrino, director, Medical Care Division, Federal Civil Defense Administration, Battle Creek, Mich.

The Scientific Method and Current Research in Inhalation Therapy, Dr. Max Sadove, head, division of anesthesiology, University of Illinois, Research and Educational Hospitals, Chicago.

Establishing the Inhalation Therapy Department at Lakewood, Dr. Walter R. Katzenmeyer, director, departments of physical medicine and inhalation therapy, Lakewood Hospital, Lakewood, Ohio.

A trip to Western Reserve University Hospital for demonstration of resuscitation and emergency therapy and display of equipment is planned. Scientific exhibits are scheduled. For information write the American Association of Inhalation Therapists, 332 South Michigan Ave., Chicago 4.

Fellowships in Respiratory Diseases.—The medical section of the National Tuberculosis Association, the American Trudeau Society, provides a limited number of fellowships to promote the training of clinicians, medical teachers, and scientific investigators in tuberculosis and respiratory diseases. Awards are open to citizens of the United States for work within this country. Candidates holding the degrees of M.D., Ph.D., or Sc.D., are eligible making possible continuation of graduate study on respiratory diseases in an approved hospital or medical center. Residency in an approved hospital under such a fellowship will be credited by the American Board of Internal Medicine toward certification in internal medicine and pulmonary diseases. Predoctoral fellowships are also offered to graduate students who hold a bachelor's degree and are working on a research project for an advanced degree other than an M.D. Each applicant must have the approval of the head of the department under whom he expects to work. Fellowships are granted for one year. Not more than two renewals will be considered. Fellowship applications must be received by Jan. 1.

A few fellowships at a higher level of training and award are offered to specially qualified candidates with an M.D. degree who have been assured of a continued teaching or research appointment upon completion of training. Trudeau fellowships are awarded for one year but may be renewed up to a total period of four years. For information write the Director of Medical Education, American Trudeau Society, c/o The Henry Phipps Institute, Seventh and Lombard Streets, Philadelphia 47, Pa.

Pediatric Residency Fellowships.—The American Academy of Pediatrics will grant 12 or more fellowships to pediatric residents for the fiscal year 1958-1959 and covering a period of six months to one year. The fellowships have been created to enable young physicians in the United States and Canada, who are in financial need, to complete their pediatric training. They carry a stipend of $500 to $1,000, depending on the length of time required to complete training and the need. The fellowships have been made possible by a grant to the academy from Mead Johnson & Company and will be granted as of July 1, 1958. The deadline for receipt of applications will be March 1, 1958. Requirements for the awards are as follows: (1) a letter from the chief of service indicating that the proposed individual will have completed by July 1, 1958, one year of pediatric residency approved by the American Board of Pediatrics; that the resident has performed his work ably; and that there is real need for financial assistance; (2) a letter from the resident requesting the fellowship stating that he intends to enter pediatric private practice at the conclusion of the residency training required for certification by the American Board of Pediatrics. Consideration will be given to geographic spread of appointments, and preference will be exhibited for well-qualified but smaller training centers. Members of the Committee of Residency Fellowships of the academy will make final decision on the granting of the awards. For information write the American Academy of Pediatrics, 1801 Hinman Ave., Evanston, Ill.

Awards in Radiological Research.—The National Academy of Sciences–National Research Council announces on behalf of the James Picker Foundation the availability of funds in support of radiological research. Applications are reviewed by the Committee on Radiology of the council's division of medical Sciences. The program is oriented toward, but not necessarily limited to, the diagnostic aspects of radiology. Support is not restricted to citizens of the United States or to laboratories within this country. Three specific types of support are offered:

(1) Grants-in-aid are designed to encourage investigations offering promise of improvement in radiological methods of diagnosis or treatment of disease. Research grants are awarded to institutions, rather than to individuals.

(2) Grants for scholars are a transitional form of support, designed to bridge the gap between the completion of fellowship training and the period when the young scientist has demonstrated his competence as an inde-

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pendent investigator. The application is submitted by the institution on behalf of the prospective scholar. If the request is approved, a grant of $6,000 per year will be made directly to the institution as a contribution toward the scholar's support, or his research, or both. Initial grants are limited to one year, but renewal for two additional years may be recommended.

(3) Fellowships in radiological research are open to candidates seeking to gain research skills leading to investigative careers in the field of radiology. Candidates whose training has been directly in the field of radiology will receive preference under this program. Candidates must hold the M.D., Ph.D., or Sc.D. degree or the equivalent. Preference will be given to applicants who are 35 years of age or less.

Applications in these three categories for the fiscal year 1958-1959 should be submitted by Dec. 1. Information may be obtained from the Division of Medical Sciences, Room 309, National Academy of Sciences–National Research Council, 2101 Constitution Ave., N. W., Washington 25, D. C.

Radioisotopes Seminar for Pathologists.—A training seminar on the diagnostic use of radioisotopes, sponsored by the American Society of Clinical Pathology and the Oak Ridge Institute of Nuclear Studies, to be held at the Medical Division, Oak Ridge, Tenn., has been set up for certified pathologists and designed to meet the requirements of the Atomic Energy Commission. This seminar will furnish an introduction to radioisotopes for those pathologists who are principally interested in diagnosis but who may be called on to assist and advise on therapeutic uses of radioisotopes. The program will consist of two one-week meetings separated by a three-month interval. The first (basic) week will consist mainly of fundamental techniques and concepts. The second (clinical) week will be held three months after the first and will be devoted mainly to the practical application of these principles. It is expected that in the intervening three months the pathologists will visit laboratories in their home areas which are already approved for the use of isotopes and will assimilate relevant literature. At the end of the second week the medical division will give to participants a statement of preceptorship in the diagnostic uses of radioisotopes. The first week will be held Nov. 11-16, 1957; the second week Feb. 10-15, 1958. Applicants must be certified in either clinical pathology or pathological anatomy, or members or fellows of the American Society of Clinical Pathology, must be United States citizens, and must have a license to practice medicine. Qualified candidates will be accepted in chronological order. Fee for the course is $25. Application should be made to Dr. Oscar B. Hunter Jr., Chairman, Council of Radioisotopes, American Society of Clinical Pathology, Suite 1000, Columbia Medical Building Annex, 915 19th Street, N. W., Washington 6, D. C. The first training seminar will be limited to 16 pathologists.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories and possessions in the weeks ended as indicated:

Area	Sept. 21, 1957 Paralytic Type	Sept. 21, 1957 Total Cases	Sept. 22, 1956 Total Cases
New England States			
Maine	....	....	....
New Hampshire	....	....	....
Vermont	....	....	2
Massachusetts	1	1	6
Rhode Island	....	....	....
Connecticut	1	1	10
Middle Atlantic States			
New York	3	5	46
New Jersey	....	6	21
Pennsylvania	....	....	19
East North Central States			
Ohio	....	9	43
Indiana	....	5	35
Illinois	6	18	63
Michigan	8	42	37
Wisconsin	3	6	38
West North Central States			
Minnesota	2	2	20
Iowa	3	9	46
Missouri	2	2	26
North Dakota	....	1	10
South Dakota	....	....	1
Nebraska	1	1	12
Kansas	....	1	13
South Atlantic States			
Delaware	....	....	3
Maryland	1	1	14
District of Columbia	5	6	1
Virginia	2	5	9
West Virginia	....	1	10
North Carolina	....	4	15
South Carolina	3	5	8
Georgia	1	2	5
Florida	2	4	14
East South Central States			
Kentucky	5	6	10
Tennessee	3	6	7
Alabama	4	7	1
Mississippi	....	....	15
West South Central States			
Arkansas	1	2	7
Louisiana	2	4	13
Oklahoma	1	5	7
Texas	5	8	27
Mountain States			
Montana	1	1	....
Idaho	....	....	2
Wyoming	....	1	1
Colorado	....	1	10
New Mexico	1	2	2
Arizona	1	2	2
Utah	....	....	22
Nevada	....	....	1
Pacific States			
Washington	....	....	5
Oregon	....	1	5
California	14	30	101
Territories and Possessions			
Alaska	....	....	....
Hawaii	1	1	....
Puerto Rico	2	2	3
Total	85	216	766

Awards for Study in Statistics.—Awards for study in statistics by persons whose primary field is not statistics but one of the physical, biological, or social sciences to which statistics can be applied are offered by the department of statistics of the University of Chicago. The awards range from $3,600 to $5,000 on the basis of an 11-month residence. The closing date for application for the academic year 1958-1959 is Feb. 15, 1958. Information may be obtained from the Department of Statistics, Eckhart Hall, University of Chicago, Chicago 37, Ill.

Meeting on Arteriosclerosis in Chicago.—The 11th annual meeting of the American Society for the Study of Arteriosclerosis will be held Nov. 2-4 at the Hotel Knickerbrocker, Chicago. There will be 62 papers presented in six sessions. The presidential address will be given the afternoon of Nov. 3 by Dr. C. F. Wilkinson Jr., New York City. The first annual G. Lyman Duff Lecture will be presented at a luncheon Oct. 3 by Dr. William Boyd, Toronto. For information write the American Society for the Study of Arteriosclerosis, P. O. Box 228, Dover, Delaware.

LATIN AMERICAN

Endocrinology Congress in Buenos Aires.—The fourth Pan American Congress on Endocrinology organized by the Argentine Society of Endocrinology and Metabolism will be held Nov. 3-9 in Buenos Aires, Argentina, under the presidency of Prof. Bernardo A. Houssay. Congress headquarters will be the Facultad de Ciencias Medicas. The scientific sessions will include lectures and scientific presentations by specially invited guest speakers. Registration fee is $15 for active members or $10 for adherent members. Scientific exhibits are planned and a program of entertainment has been arranged. For information write the Fourth Pan American Congress of Endocrinology, Tesorero, Asociacion Medical Argentina, Santa Fe 1171, Buenos Aires, Argentina.

EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

AMERICAN BOARD OF ANESTHESIOLOGY: *Oral.* Washington, Oct. 28-Nov. 1. Various locations in the United States and Canada, July 18. Final date for filing application is Jan. 18. Sec., Dr. Curtiss B. Hickcox, 80 Seymour St., Hartford 15.

AMERICAN BOARD OF DERMATOLOGY: *Oral.* Baltimore, Oct. 11-13. Final date for filing application was April 1. Sec., Dr. Beatrice Maher Kesten, One Haven Ave., New York 32.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* Oct. 21. *Oral.* Los Angeles, Sept. 11-14. Final date for filing applications was Feb. 1. Exec. Sec., Dr. W. A. Werrell, 1 West Main St., Madison 3, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. Sec., Dr. Leonard T. Furlow, Washington University School of Medicine, St. Louis 10.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY. Various locations in the United States and Canada. *Part I.* Jan. 2. *Part II.* Chicago, May 7-17. Final date for filing application is September 1. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

AMERICAN BOARD OF OPHTHALMOLOGY: *Oral.* Chicago, Oct. 7-11. *Written.* January 1958. Final date for filing application was July 1. Sec., Dr. Merrill J. King, Box 236, Cape Cottage Branch, Portland 9, Maine.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Part I.* April 3-4, Rochester, Minnesota, Denver, Colorado, Washington, D. C. Final date for filing application is Nov. 30. *Part II.* New York City, Jan. 29-31, 1958. Sec., Dr. Sam W. Banks, 116 South Michigan Avenue, Chicago 3.

AMERICAN BOARD OF OTOLARNGOLOGY: Chicago, Oct. 7-11. Final date for filing application was in April. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

AMERICAN BOARD OF PATHOLOGY: *Oral and Written. Pathologic Anatomy and Clinical Pathology.* New Orleans, Sept. 26-28. Final date for filing application is August 15. Sec., Dr. Edward B. Smith, Indiana University Medical Center, Indianapolis 7.

AMERICAN BOARD OF PEDIATRICS: *Oral.* Chicago, Oct. 11-13. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

AMERICAN BOARD OF PLASTIC SURGERY: *Oral and Written Examination.* San Francisco, Oct. 31-Nov. 2. Final date for filing case reports was July 1. Corresponding Sec., Miss Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8.

AMERICAN BOARD OF PREVENTIVE MEDICINE: *In Public Health. Oral and Written.* Cleveland, Nov. 7-9. Sec., Dr. Thomas F. Whayne, 3438 Walnut St., Philadelphia.

AMERICAN BOARD OF PROCTOLOGY: *Oral and Written. Parts I and II.* September. Sec., Dr. Stuart T. Ross, 520 Franklin Ave., Garden City, N. Y.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New York, Dec. 16-17. San Francisco, March 17-18. Sec., Dr. David A. Boyd, Jr., 102-110 Second Ave., S. W., Rochester Minn.

AMERICAN BOARD OF RADIOLOGY: Washington, Sept. 23-28. Final date for filing application was June 1. Chicago, May 20-24. Final date for filing application is Jan. 1, 1958. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Part II.* Buffalo, Sept. 23-24; New Haven, Oct. 21-23; Indianapolis, Nov. 18-19; Cincinnati, Dec. 16-17; New Orleans, Jan. 13-14; Durham, N. Car., Feb. 10-11; Baltimore, March 10-11; Chicago, May 12-13; Los Angeles, June 16-17 and Portland, Oregon, June 20-21. Sec., Dr. John B. Flick, 22' So. 15th St., Philadelphia 2.

AMERICAN BOARD OF UROLOGY: *Written examination.* Various cities throughout the country. *Pathology and Oral Clinical.* February 1958. Location not decided. Exec. Secretary, Mrs. Ruby L. Griggs, 30 Westwood Road, Minneapolis 16.

BOARD OF THORACIC SURGERY: *Written.* Various centers throughout the country, Sept. 6, and the closing date for registration was July 1, 1957. Sec., Dr. William H. Tuttle, 1151 Taylor Ave., Detroit 2.

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GOVERNMENT SERVICES

AIR FORCE

Consultants Visit Medical Installations.—Five national consultants to the surgeon general recently visited Air Force medical installations in Europe, Alaska, and the Far East. In line with the surgeon general's policy, they rendered services on problem cases in their specialties and conducted lectures and teaching sessions.

Dr. Elmer Hess visited installations in England, France, Germany, Greece, Turkey, Saudi Arabia, and Tripoli. Dr. Hess, a past-president of the American Medical Association, has been appointed chairman of the Health Resources Advisory Committee, Office of Defense Mobilization, and chairman of the National Advisory Committee, Selective Service System.

Dr. Arthur Grollman, chairman, department of experimental medicine, Southwestern Medical School, University of Texas, and Dr. James H. Allen, chairman of the department of ophthalmology, University of Tulane School of Medicine, visited installations in Japan, Korea, Okinawa, Hawaii, and the Philippine Islands.

Dr. Clair M. Kos, professor of otolaryngology, Iowa College of Medicine, State University of Iowa, and Dr. Robert J. Coffey, professor of surgery, Georgetown University School of Medicine, visited installations in Alaska.

Awards.—Major Gen. William H. Powell Jr., former deputy surgeon general of the U. S. Air Force, and now senior medical officer at Supreme Headquarters Allied Powers, Europe, has been awarded a Legion of Merit for his "significant efforts, as military leader and physician . . . in raising the United States Air Force Medical Service to an unprecedented level of professional competence . . . with its resultant contribution to the operational capability of the Air Force."——Major Gen. Olin F. McIlnay, deputy surgeon general of the U. S. Air Force has received the First Oak Leaf Cluster to the Legion of Merit. General McIlnay was cited for exceptionally meritorious conduct in the performance of outstanding service while serving as director of plans and hospitalization in the office of the surgeon general, U. S. Air Force, from June, 1952, to June, 1957. He modernized the budget and fiscal policies of the plans and hospitalization division, and through improving logistical planning for both mobilization and daily operations, contributed materially to the safety of the nation.

Personal.—Lieut. Col. George R. Steinkamp has been appointed head of the department of space medicine at the Air Force School of Aviation Medicine, Randolph Air Force Base, Texas, succeeding Dr. Hubertus Strughold, who founded the department in 1949. Dr. Strughold has been appointed advisor for research to Major Gen. Otis O. Benson Jr., commandant of the school at Randolph Air Force Base.

NAVY

Foreign Officers Attend U. S. Naval School.—Thirty foreign naval medical officers, representing NATO and SEATO nations, are assigned to postgraduate training, of two months' duration, at the Naval Medical School, Bethesda, Md., commencing Sept. 16. This training is under U. S. Navy sponsorship in accordance with the Mutual Security Act of 1954, under the provisions of the Military Assistance Program.

VETERANS ADMINISTRATION

Personal.—Dr. Albert L. Olsen, director, professional services, VA Hospital, Battle Creek, Mich., will be transferred as manager of the Knoxville, Iowa, VA Hospital, to succeed the late James R. Jack.

Dr. Henry L. Vogl, director, professional services, VA Center, Wood, Wis., will be transferred as manager of the VA Hospital in Minneapolis, replacing Dr. John A. Seaberg, who retired recently.

The hospital at Knoxville is a 1,540-bed neuropsychiatric hospital, and the Minneapolis institution is a 973-bed general medicine and surgery hospital.

Dr. Thomas L. Auth, chief, neurology service, VA Hospital, Washington, D. C., has been appointed chief of the neurology division at the VA Central Office in Washington, succeeding Dr. Benedict Nagler, who left the Veterans Administration Sept. 8 to become superintendent of the Lynchburg Training School and Hospital at Colony, Va. Dr. Auth is certified in neurology by the American Board of Psychiatry and Neurology and is on the teaching staff of Georgetown University School of Medicine. ——Dr. Benjamin F. Jackson, manager, VA Hospital, Tomah, Wis., will be transferred as manager of the VA Hospital at Bedford, Mass. Dr. Thomas E. Dredge, director, professional services, VA Hospital, St. Cloud, Minn., will succeed Dr. Jackson as manager of the Tomah hospital. The position of manager at the Bedford hospital was vacant because of retirement of Dr. Winthrop Adams, May 31, 1957. The Bedford and Tomah hospitals serve veterans with predominantly neuropsychiatric disorders.

Dr. Chamberlain Heads Atomic Program.—Dr. W. Edward Chamberlain, professor emeritus of radiology, Temple University Medical School, and president of the American Roentgen Ray Society, will head the Veterans Administration atomic medicine program in Washington, D. C., the VA announced Sept. 16. He will serve as special assistant for atomic medicine to the VA Chief Medical Director, Dr. William S. Middleton, and as associate director of the VA research service.

Dr. Chamberlain was director of the Temple University Hospital, department of radiology, and professor of radiology at Temple University Medical School, Philadelphia, from 1930 to February, 1957. He was head of the department of radiology at Stanford University Hospital from 1920 to 1930, professor of medicine in charge of radiology at the Stanford University Medical School from 1926 to 1930, and in private practice as a radiologist in San Francisco from 1919 to 1930. From 1917 to 1919, he served in the Navy as a lieutenant (j. g.) at the Mare Island Naval Hospital and in Scotland.

Seminar on Tranquilizers.—On Sept. 18, at the Northport Veterans Hospital, a seminar on tranquilizing drugs was presented by the Suffolk County Medical Society in affiliation with the VA Hospital, Northport, Long Island, N. Y., and the Dean's Committe of the State University of New York, College of Medicine. The speakers were Dr. David M. Engelhardt, associate professor of psychiatry, State University of New York, College of Medicine, "Outpatient Treatment of Schizophrenics with Ataractics," Dr. Henry Brill, assistant commissioner, State of New York, Department of Mental Hygiene, Albany, N. Y., "Clinical Research with Ataractic Drugs," and Dr. Frank Berger, director of medical research, Wallace Laboratories, New Brunswick, N. J., "The Tranquilizers—A Critical Review."

PUBLIC HEALTH SERVICE

New Research Training Program.—The Public Health Service has announced a new program of financial support for advanced training of research scientists in the field of neurological and sensory disorders to be conducted by the National Institute of Neurological Diseases and Blindness. A previous program, under which about 75 scientists received advanced training during the last fiscal year, was concerned exclusively with clinical training. The new program is designed to encourage advanced training in either the clinical area or in such basic science areas as neurochemistry, neuropharmacology, neurophysiology, or neuroanatomy.

While individual awards under the program generally will be made for not less than nine months and for not more than one year, all awards are subject to renewal and may be continued for three years. Stipends are determined in accordance with the applicant's qualifications and training needs and may range from $5,500 to $14,800 a year.

Application forms may be obtained from the Chief, Extramural Programs Branch, National Institute of Neurological Diseases and Blindness, Bethesda 14, Md.

Applicants must be citizens of the United States and free of any physical or mental disability that would interfere with the proposed training. They must have completed either (1) the residency training requirements in a clinical specialty, or its equivalent, or (2) at least three years of pertinent postdoctoral training or research experience.

Special traineeships may be awarded for training at any institution in the United States or abroad qualified to give the particular training desired by the applicant. The trainee may begin training at any time within 10 months of the date of his award. During the period of training, the trainee will not be permitted to carry on the private practice of medicine, and he may engage only in such teaching, clinical, and research activities as are a prescribed part of his training program.

Neuropharmacology Research Center.—Dr. Joel J. Elkes, British pharmacologist, has been appointed to the staff of the National Institute of Mental Health, to head a newly organized clinical neuropharmacology research center at St. Elizabeths Hospital, Washington, D. C., which will be jointly operated by the institute and the hospital.

Dr. Elkes, former chairman, department of experimental psychiatry, University of Birmingham, England, has concentrated his research in chemistry and the pharmacology of the nervous system for the past six years. During this period he has also been scientific director of the Early Treatment Research Hospital in Birmingham. He received his education at St. Mary's Hospital Medical School of the University of London. He has been the Sir Halley Stewart Research Fellow in the department of pharmacology at the University of Birmingham. During the period between 1950 and 1951, on a Fulbright traveling grant, he traveled in the United States.

Dr. Elkes has been a member of the research committee of the Mental Health Research Fund of Great Britain, and also was the organizing secretary of the First International Neurochemical Symposium, held at Oxford in 1954.

Dr. MacLean Joins National Institute of Mental Health.—Dr. Paul D. MacLean, formerly associate professor of physiology, Yale University School of Medicine, has joined the staff of the National Institute of Mental Health, Bethesda, Md., as chief, section on limbic integration and behavior, basic research branch.

Over the last 10 years, Dr. MacLean's analysis of the neurophysiology of the phylogenetically old (limbic) cortex and its connections with other brain structures has led to the development of theories relating to emotional behavior. He has related these neurophysiological mechanisms to temporal lobe epilepsy and its associated unconscious movements. In his new position, Dr. MacLean will continue to investigate the role of the "old" cortex and its associated structures (limbic system) in emotional, visceral, and other forms of behavior.

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DEATHS

Matas, Rudolph ✦ New Orleans, surgeon and first recipient of the Distinguished Service Medal of the American Medical Association in 1938, died in the Touro Infirmary Sept. 23, aged 97. Dr. Matas was born Sept. 12, 1860, at Bonnet Carre, La. His early education was acquired in Barcelona, Paris, Brownsville, Texas, and New Orleans. He graduated at the University of Louisiana Medical Department in New Orleans in 1880, and served an internship at Charity Hospital. In 1879 Dr. Matas accompanied the yellow fever commission of the National Board of Health to Havana, Cuba. He began the practice of medicine in New Orleans in 1880, became chief of the clinic of surgery and gynecology at his alma mater, later known as Tulane University of Louisiana, serving until 1886. From 1895 to 1927 he was professor of surgery at Tulane University. He is said to have introduced the first spinal anesthetic in this country at Charity Hospital. Dr. Matas was organizer of Base Hospital 24 (Tulane Unit) for service in France, 1916-1917. Dr. Matas was a past-president of the New Orleans Medical and Surgical Society, the Louisiana State Medical Society, the American Surgical Association, the Southern Surgical Society, American Association of Thoracic Surgeons, the American College of Surgeons, and the International Society of Surgery. He was a member of the founders group of the American Board of Surgery. He was decorated by the governments of Venezuela, Spain, France, and Cuba. Tulane dedicated its medical library to Dr. Matas in 1937. He was co-inventor of the Matas–Smythe pump for artificial respiration. Named after him are the Rudolph Matas Award in Vascular Surgery, and an annual lecture sponsored by the Nu Sigma Nu medical fraternity at Tulane. In 1903 he was a member of the House of Delegates of the American Medical Association, serving as chairman of the Section on Surgery and Anatomy in 1907, and as Vice-President in 1921 and again in 1932-1933. A prolific contributor to the medical literature, Dr. Matas' attainments also encompassed the arts of music, painting, and sculpture. He received honorary degrees from Washington University, the University of Alabama, Tulane University, the University of Pennsylvania, Princeton, and the National University of Guatemala.

Lowrey, Lawson Gentry, New York City; born in Centralia, Mo., Dec. 23, 1890; Harvard Medical School, Boston, 1915; served on the faculties of the University of Utah in Salt Lake City, University of Missouri in Columbia, Harvard in Boston and Columbia University in New York City; lectured on psychiatry at the State University of Iowa in Iowa City, Southern Methodist University, Dallas, Texas, Smith College, Northampton, Mass., Hunter College in New York City, University of Minnesota, Minneapolis, and Western Reserve University School of Applied Social Sciences, Cleveland; in 1927 left Cleveland and came to New York, where he directed the new Institute of Child Guidance; served as psychiatrist in this area for several hospitals, the board of education and the Traveler's Aid Society; pathologist at the Danvers (Mass.) State Hospital from 1914 to 1917, when he became chief medical officer of the Boston Psychopathic Hospital, serving until 1920; served as assistant director of the Iowa State Psychopathic Hospital in Iowa City, consultant in psychiatry at the Grasslands Hospital in Valhalla, N. Y., and for many years attending psychiatrist for the Vanderbilt Clinic; specialist certified by the American Board of Psychiatry and Neurology; member of the Medical Society of the State of New York, American Psychiatric Association, and the American Psychopathological Association; past-president of the American Orthopsychiatric Association; served as a member of the executive committee of international conference on mental health; for many years editor of the *American Journal of Orthopsychiatry;* author of "Psychiatry for Social Workers" and others; served as associate editor of the *American Journal of Psychiatry;* died in the Knickerbocker Hospital Aug. 16, aged 66.

Lillie, Harold Irving ✦ Rochester, Minn.; born in Grand Haven, Mich., May 6, 1888; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1912; interned at the University of Michigan Hospital in Ann Arbor; an instructor in otolaryngology at his alma mater from 1913 to 1915 when he moved to Chicago, where he served as an instructor in otolaryngology at Rush Medical College in 1916-1917; in April, 1917, came to the Mayo Clinic, where on July 1, 1917, the section on otolaryngology and rhinology was established and he became the first head of the new unit; held that post until he became a senior consultant on Oct. 1, 1951; retired from the Mayo Clinic July 1, 1953; was professor of otolarygology and rhinology in the Mayo Foundation, Graduate School, University of Minnesota, where he held the title of emeritus professor of otolaryngology; president of the American Laryngological, Rhinological, and Otological Society in 1939 and of the American Laryngological Society in 1945-1946; fellow of the American Col-

✦ Indicates Member of the American Medical Association.

lege of Surgeons and of the International College of Surgeons; member of the Southern Minnesota Medical Association, Minnesota Academy of Ophthalmology and Otolaryngology, American Academy of Ophthalmology and Otolaryngology, American Otological Society, Alumni Association of the Mayo Foundation, Alpha Omega Alpha, Sigma Xi, and the Phi Beta Pi; life member of the University of Michigan Union; specialist certified by the American Board of Otolaryngology; died Aug. 27, aged 69, of emphysema.

Dieckmann, William Joseph ✱ Chicago; born in Belleville, Ill., Oct. 20, 1897; Washington University School of Medicine, St. Louis, 1922; joined the faculty of his alma mater as instructor in the department of obstetrics in 1924, subsequently becoming assistant professor of obstetrics and associate professor of obstetrics and gynecology; while in St. Louis served on the staffs of the Barnes Hospital from 1924 to 1931 and St. Louis Maternity Hospital from 1927 to 1931 when he became associate professor of obstetrics and gynecology at the University of Chicago, The School of Medicine; in 1942 became Mary Campau Ryerson professor of obstetrics and gynecology at the University, and from October, 1942, until January, 1954, was chairman of the department and chief of the staff at the Chicago Lying-In Hospital; specialist certified by the American Board of Obstetrics and Gynecology; past-president and vice-president of the Chicago Gynecological Society; member of the American Association of Obstetricians and Gynecologists, American Gynecological Society, Central Society for Clinical Research, Society for Experimental Medicine and Biology, and the Endocrine Society; attending gynecologist at the Albert Merritt Billings Hospital; editor of the *American Journal of Obstetrics and Gynecology;* recently completed the third revision of his book "The Toxemias of Pregnancy"; died Aug. 15, aged 59, of myocardial infarction and arteriosclerotic cardiovascular disease.

Ellis, Edward Forrest ✱ Fayetteville, Ark.; born Aug. 18, 1863; Missouri Medical College, St. Louis, 1885; member of the House of Delegates of the American Medical Association in 1930-1931; past-president of the Washington County Medical Society, Arkansas State Medical Society, Frisco Medical Association, and the Tenth Councilor District Medical Society; member of the American Association of Railway Surgeons; fellow of the American College of Surgeons and the International College of Surgeons; a member of the state board of medical examiners during two gubernatorial administrations; chief of staff of the City Hospital, where he was a staff member since the founding in 1912; for many years member of the school board; a charter member of the board of directors of the First National Bank; awarded an honorary LL.D. degree from the University of Arkansas in 1934; the Ellis Room in the library of the University of Arkansas School of Medicine in Little Rock houses a professional library of more than 1,100 books presented by Dr. Ellis; the Washington County Historical Society presented him with a "Distinguished Citizen" citation on his 90th birthday; died Aug. 7, aged 93, of heart block.

Osborn, John Ernest ✱ Rochester, Minn.; born in Wolcott, N. Y., Aug. 11, 1918; University of Buffalo School of Medicine, 1943; interned at the Rochester (N. Y.) General Hospital; certified by the National Board of Medical Examiners; specialist certified by the American Board of Anesthesiology; president of the Minnesota Society of Anesthesiologists; member of the American Society of Anesthesiologists, International Anesthesia Research Society, Alumni Association of the Mayo Foundation, Alpha Chi Sigma, and Nu Sigma Nu; fellow of the American College of Anesthesiologists and of the International College of Anesthetists; an honorary member of the Cuban Society of Anesthesiologists; came to Rochester in September 1944 as a fellow in anesthesiology of the Mayo Foundation; in the medical corps of the Army of the United States from 1946 to 1948 and returned to the Mayo Foundation to resume his fellowship; in 1956 appointed an instructor in anesthesiology in the Mayo Foundation, Graduate School, University of Minnesota; consultant in anesthesiology at the Mayo Clinic since 1949; on the staff of St. Mary's Hospital, where he died July 30, aged 39, of cancer.

Biro, Louis P., ✱ Los Angeles; born in Budapest, Hungary Nov. 5, 1890, University of Pennsylvania School of Medicine, Philadelphia, 1920; specialist certified by the American Board of Physical Medicine and Rehabilitation; member of the American Society of Physical Medicine and Rehabilitation; formerly instructor of physical medicine at the New York Polyclinic Medical School and Hospital and on the staff of the Goldwater Memorial Hospital in New York City; served as lecturer of physical medicine at the University of Southern California School of Medicine; on the staffs of the Santa Monica (Calif.) Hospital and the California Hospital, where he died July 23, aged 66, of myocardial infarction.

Wedemeyer, Marlin Richard ✱ Columbus, Ohio; born in Gallipolis, Ohio, June 7, 1908; Ohio State University College of Medicine, Columbus, 1933; member of the American Psychiatric Association; at one time practiced in Oak Hill and served as vice-president of the Jackson County Medical Society; veteran of World War II; formerly director of counseling and diagnostic clinic at the Ohio Penitentiary; in 1951 was named director of the Toledo Mental Hygiene Center, where he remained until his appointment as superintendent of the Co-

lumbus State Hospital, serving until his death at the University Hospital July 30, aged 49, of cardiovascular arteriosclerosis and pneumonia.

Smith, Roy Kenneth, Duarte, Calif.; born in 1885; University of Kansas School of Medicine, Kansas City, 1911; also an ordained minister; fellow of the American College of Physicians; member of the American Trudeau Society; specialist certified by the American Board of Internal Medicine; service member of the American Medical Association; served as a medical missionary in Korea; formerly resident physician at the State Sanatorium for Tuberculosis in Norton, Kan., and chief of the tuberculosis service of the Veterans Administration Hospital in Excelsior Springs, Mo.; died in Collis P. and Howard Huntington Memorial Hospital in Pasadena, July 31, aged 72.

Olds, William Henry ✦ Los Angeles; born in Sprague, Wash., in 1886; Rush Medical College, Chicago, 1912; emeritus professor of surgery at the College of Medical Evangelists; member of the founders group of the American Board of Surgery; fellow of the International College of Surgeons and the American College of Surgeons; on the consulting staffs of the Orthopedic Hospital and the Santa Monica (Calif.) Hospital; associated with the Los Angeles County Hospital; served as chief of the surgical staff, California Hospital, where he was a member of the executive medical board, and where he died July 31, aged 70, of coronary disease.

Ball, Peter ✦ Baltimore; born in Berlin, Germany, July 6, 1923; Columbia University College of Physicians and Surgeons, New York City, 1950; certified by the National Board of Medical Examiners; interned at the Bellevue Hospital in New York City, where he served a residency; formerly a resident at the Presbyterian Hospital, New York City, and the U. S. Public Health Service Hospital; at one time associated with the U. S. Public Health Service Reserve and the Indian Service; died in the U. S. Public Health Service Hospital, July 7, aged 34.

Smith, Scott Lord ✦ Poughkeepsie, N. Y.; born in 1878; Columbia University College of Physicians and Surgeons, New York City, 1906; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; member of the House of Delegates of the American Medical Association from 1945 to 1951; served as second vice-president of the Medical Society of the State of New York; past-president of the Dutchess County Medical Society; served as trustee and president of the Vassar Brothers Hospital, where he died July 30, aged 78, of cerebral hemorrhage.

Lang, Valorus Frederick ✦ Milwaukee; Northwestern University Medical School, Chicago, 1930; assistant clinical professor of occupational and environmental medicine at Marquette University School of Medicine; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; member of the board of directors of the Central Agency for Chronically Ill; on the staffs of the Milwaukee Hospital and Columbia Hospital, where he died Aug. 2, aged 51, of arteriosclerotic heart disease.

Turner, Ewing Lee ✦ Los Angeles; Rush Medical College, Chicago, 1934; assistant clinical professor of surgery at University of California School of Medicine; fellow of the American College of Surgeons; specialist certified by the American Board of Surgery; veteran of World War II; trustee and past-president of the Los Angeles County Medical Association; a member of the staff at Good Samaritan Hospital; surgeon for the Union Pacific Railroad; died in San Diego July 24, aged 51, of myocardial infarction.

Risser, Arthur Strohm, Blackwell, Okla.; University Medical College of Kansas City, Mo., 1905; an associate member of the American Medical Association, serving as a member of its House of Delegates from 1941 to 1944; past-president of the Oklahoma State Medical Association; fellow of the American College of Surgeons; associated with the Blackwell General Hospital, where he served as president of the medical staff and where he died July 17, aged 80.

Stormont, Riley McMillan ✦ Webb City, Mo.; born Dec. 2, 1874; Kentucky School of Medicine, Louisville, 1898; past-president of the Jasper County Medical Society; formerly county coroner; plant physician for the DuPont Powder Company for many years; local physician for the Frisco Railroad and Missouri Pacific Railroad; on the staffs of the Freeman Hospital and St. John's Hospital in Joplin and the McCune–Brooks Hospital in Carthage; died July 24, aged 82, of cerebral hemorrhage.

Werelius, Axel F. W. ✦ Chicago; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1902; fellow of the American College of Surgeons; in 1920 knighted by King Gustav V of Sweden for his medical work; co-founder and formerly chief of surgical staff of South Shore Hospital; member of the surgical staff, Illinois Central Hospital, where he died Aug. 8, aged 86, of arteriosclerosis and gangrene of the left leg.

Barringer, Paul Ernest, East Meadow, N. Y.; Minneapolis College of Physicians and Surgeons, 1907; died June 30, aged 72, of bronchopneumonia and carcinoma of the prostate.

Berry, Mary Ella Kirby, Jorhat, Assam, India; Temple University School of Medicine, Philadelphia, 1942; interned at Lancaster (Pa.) General Hospital;

certified by the National Board of Medical Examiners; medical missionary; died Aug. 2, aged 41, of Asian influenza and leukopenia.

Brown, Paul ✦ Baltimore; University of Maryland School of Medicine, Baltimore, 1909; died in the Maryland General Hospital May 25, aged 72.

Bryson, Roy Douglas ✦ Callaway, Neb.; Lincoln Medical College of Cotner University, 1907; veteran of World War I; a member of the Chamber of Commerce and for many years served on the board of education; died in the Callaway Municipal Hospital July 19, aged 74, of uremia and coronary occlusion.

Bumstead, John Henry ✦ New Haven, Conn.; Johns Hopkins University School of Medicine, Baltimore, 1923; associate clinical professor of medicine at Yale University School of Medicine; veteran of World Wars I and II; on the staff of the Grace-New Haven Community Hospital; died July 29, aged 60, of acute myocardial infarction.

Burke, Emilie Elizabeth Mundy ✦ Havertown, Pa.; Woman's Medical College of Pennsylvania, Philadelphia, 1923; member of the American Academy of General Practice; on the staffs of the Misericordia Hospital in Philadelphia and the Thomas M. Fitzgerald Mercy Hospital in Darby, where she died July 31, aged 60.

Buten, Edward J., Fort Thomas, Ky.; Eclectic Medical Institute, Cincinnati, 1907; died June 22, aged 75, of arteriosclerotic heart disease with decompensation.

Dodson, Hobart W., Pompano Beach, Fla.; Jefferson Medical College of Philadelphia, 1921; practiced in Nanticoke, Pa.; died July 28, aged 60.

Donath, Lawrence Herbert ✦ Wauwatosa, Wis.; Marquette University School of Medicine, Milwaukee, 1933; veteran of World War II; served as health officer of Lake Geneva; on the staff of St. Mary's Hospital, Milwaukee, where he died July 23, aged 51, of carcinoma of the lung.

Douglass, Alvin E., DeQuincy, La.; Memphis (Tenn.) Hospital Medical College, 1909; formerly member of the town council; Ward six police juror; died in St. Patrick's Hospital, Lake Charles, July 24, aged 72.

Farthing, J. Watts ✦ Wilmington, N. C.; University of Pennsylvania School of Medicine, Philadelphia, 1933; certified by the National Board of Medical Examiners; member of the Southeastern Surgical Congress; fellow of the American College of Surgeons; associated with the James Walker Memorial Hospital and the Community Hospital; died in Lexington, Ky., July 27, aged 48, of emphysema and bronchial asthma.

Forrest, James Finley ✦ Summit Hill, Pa.; Jefferson Medical College of Philadelphia, 1917; veteran of World War II; died June 24, aged 65, of amytrophic lateral sclerosis.

Hall, George Washington ✦ Northport, Ala.; Birmingham Medical College, 1914; served overseas during World War I; died in Birmingham, July 27, aged 74.

Hall, James Roland ✦ Kansas City, Mo.; College of Physicians and Surgeons, Medical Department of the Kansas City University, Kansas City, Kan., 1904; died July 24, aged 88, of cardiovascular renal disease.

Hand, Patrick James ✦ Glenolden, Pa.; University of Pennsylvania School of Medicine, Philadelphia, 1935; member of the Industrial Medical Association; died in Avalon, N. J., July 23, aged 48, of coronary occlusion.

Harris, Marcus Lafayette ✦ Newport, Ark.; University of Louisville (Ky.) Medical Department, 1910; member of the state board of medical examiners; past-president of the school board; associated with the Harris Hospital; died July 23, aged 75, of a heart attack.

Hart, Raymond Lochary, Kearney, Neb.; State University of Iowa College of Medicine, Iowa City, 1897; served on the city council; formerly president of the First National Bank in Amherst; past-president of the Nebraska State Medical Association and the Kearney Rotary Club; died July 31, aged 84, of a heart attack.

Hawkins, Andrew Peter, Waubay, S. D.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1904; an associate member of the American Medical Association; veteran of World War I; died in the Peabody Hospital in Webster June 28, aged 79, of pernicious anemia.

Heyerdale, Oscar C. ✦ Rochester, Minn.; Northwestern University Medical School, Chicago, 1898; served on the staff of the Rochester State Hospital; died July 20, aged 85, of fracture-dislocation of cervical spine due to a fall.

Hitschmann, Edward E., Cambridge, Mass.; Medizinische Fakultät der Universität, Vienna, Austria, 1895; member of the American Psychoanalytic Association; joint author of "Frigidity in Women: Its Characteristics and Treatment"; died July 31, aged 86.

Hodgkins, Albert E., Stockton, Calif.; L. R. C. P., of London, and M. R. C. S., of England, 1898; during World War I served 18 months in the Royal Army Medical Corps; died July 10, aged 85, of erysipelas.

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Houston, Donald McClure ✦ Park Rapids, Minn.; University of Minnesota Medical School, Minneapolis, 1935; certified by the National Board of Medical Examiners; veteran of World War II; on the staff of St. Joseph's Hospital, where he died June 20, aged 49, of cerebral hemorrhage.

Huffman, Albert Dale ✦ Acton, Ind.; Indiana University School of Medicine, Indianapolis, 1917; served as president of St. Joseph County Medical Society; veteran of World War I; died June 15, aged 73, of coronary occlusion.

Klein, Samuel Moses ✦ Flushing, N. Y.; University and Bellevue Hospital Medical College, New York City, 1920; veteran of World Wars I and II; served on the staff of the Kew Gardens (N. Y.) Hospital; fellow of the American College of Surgeons; died July 23, aged 60, of coronary thrombosis.

Klock, Egbert Le Roy, Orwigsburg, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1905; member of the Medical Society of the State of Pennsylvania; served as deputy coroner and school physician; on the staffs of the Good Samaritan Hospital and the Pottsville Hospital in Pottsville where he died July 29, aged 76, of carcinoma of the prostate.

Kremser, Valentine Charles ✦ Amery, Wis.; Marquette University School of Medicine, Milwaukee, 1934; member of the American Academy of General Practice; served as city health officer; on the staff of the Apple River Memorial Hospital, where he died July 12, aged 49, of a heart attack.

Larner, Arthur Leo ✦ Burlington, Vt.; University of Vermont College of Medicine, Burlington, 1904; served on the faculty of his alma mater; veteran of World War I; during World War II received the medal certificate of merit for volunteer work in Selective Service; on the staffs of the Mary Fletcher Hospital and the Bishop De Goesbriand Hospital, where he died July 24, aged 75, of a cerebral vascular accident.

Largay, Arthur Owen ✦ Bayonne, N. J.; Georgetown University School of Medicine, Washington, D. C., 1917; veteran of World War I; served as school physician; member of the staffs of the Bertold S. Pollak Hospital for Chest Diseases and the Greenville Hospital in Jersey City and the Bayonne Hospital; died Aug. 2, aged 66, of carcinoma of the recto-sigmoid.

Lerner, Leiber Wolfe ✦ Miami, Fla.; McGill University Faculty of Medicine, Montreal, Quebec, Canada, 1919; fellow of the American College of Surgeons; on the courtesy staffs of Victoria Hospital and the Mercy Hospital, where he died July 4, aged 59, of myocardial infarction.

McCooey, Daniel F., Dover, N. H.; McGill University Faculty of Medicine, Montreal, Que., Canada, 1935; certified by the National Board of Medical Examiners; veteran of World War II; on the staff of the Wentworth–Dover City Hospital; died July 28, aged 51, of nephritis.

McHale, Joseph John, Washington, D. C.; Georgetown University School of Medicine, Washington, 1924; veteran of World War I; served on the staffs of the Georgetown and District of Columbia General hospitals, and Columbia Hospital for Women and Lying-In Asylum; died Aug. 3, aged 58, of coronary thrombosis.

Mason, Mary Taylor, Philadelphia; Woman's Medical College of Pennsylvania, Philadelphia, 1915; died in the Germantown Dispensary and Hospital Aug. 13, aged 86, of bronchopneumonia, cardiac failure, and fracture of the hip.

Micklethwait, Oscar Richard ✦ Portsmouth, Ohio; Medical College of Ohio, Cincinnati, 1906; on the staffs of the Portsmouth General Hospital and the Mercy Hospital, where he died July 31, aged 75, of acute myocardial infarction.

Miller, H. Edward ✦ St. Louis; Washington University School of Medicine, St. Louis, 1902; specialist certified by the American Board of Otolaryngology; member of the American Laryngological, Rhinological and Otological Society; served on the faculty of his alma mater; consulting otolaryngologist at Lutheran Hospital; died in the Evangelical Deaconess Hospital Aug. 3, aged 79.

Moras, Edmond Raymond, Libertyville, Ill.; Harvard Medical School, Boston, 1888; College of Physicians and Surgeons of Chicago, 1889; for many years practiced in Highland Park; died in St. Therese Hospital, Waukegan, Aug. 3, aged 92.

Morris, Isaac Cahal, Bull Shoals, Ark.; Memphis (Tenn.) Hospital Medical College, 1906; died in Fayetteville July 25, aged 78, of carcinoma of the ampulla of vater.

Moyer, Rita Slater ✦ Lockport, N. Y.; University of Buffalo School of Medicine, 1935; formerly school physician; city health officer; on the staff of the Lockport Memorial Hospital; died in the Buffalo (N. Y.) General Hospital June 19, aged 43, of hepatitis.

Pfister, Faris Fred ✦ Webster, S. D.; University of Cincinnati College of Medicine, 1924; member of the American Academy of General Practice; president of the state board of medical examiners; served as vice-president of the South Dakota State Medical Association; for many years member of the school board, of which he was past-president; on the staff of the Peabody Memorial Hospital; died July 30, aged 55, of hypertension.

Price, Charles Wesley, Daytona Beach, Fla.; Vanderbilt University School of Medicine, Nashville, Tenn., 1915; served on the staff of the Essex County Overbrook Hospital in Cedar Grove, N. J. and the Central State Hospital in Nashville, Tenn.; died Aug. 1, aged 71, of arteriosclerotic heart disease.

Raibourn, Richard Lorenzo, Princeton, Ind.; Dunham Medical College, Chicago, 1902; formerly on the staff of the Veterans Administration Hospital in Hot Springs, S. D.; died in the Gibson General Hospital July 7, aged 79, of virus pneumonia.

Reiff, Melville Newton ✦ Washington C. H., Ohio; Western Reserve University School of Medicine, Cleveland, 1931; coroner of Fayette County; on the staff of the Fayette County Memorial Hospital, where he died July 30, aged 52, of coronary disease followed by pneumonia.

Reiss, Alexander ✦ Monroe, N. Y.; Fordham University School of Medicine, New York City, 1919; served on the staffs of the Cornwall (N. Y.) Hospital and the Goshen (N. Y.) Hospital; died July 5, aged 65, of coronary thrombosis.

Richardson, David Phillip, Union, Okla.; Louisville (Ky.) Medical College, 1894; an associate member of the American Medical Association; also a druggist; served as postmaster; on the staff of the Wesley Hospital; died July 13, aged 88, of heart disease.

Ritchie, Douglas William ✦ Temple City, Calif.; University of Oregon Medical School, Portland, 1926; veteran of World Wars I and II; interned at the Los Angeles County General Hospital, where he was assistant medical director; for many years medical director of the Rancho Los Amigos Hospital in Hondo; died July 26, aged 62, of coronary arteriosclerosis.

Robb, Winifred Arene Yelton ✦ Newton, Ill.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1901; past-president of the Jasper County Medical Society; died July 24, aged 85.

Romano, Anthony Mario, Tenafly, N. J.; Georgetown University School of Medicine, Washington, D. C., 1933; member of the Medical Society of New Jersey and the American Society of Anesthesiologists; died Aug. 1, aged 48, of pulmonary edema.

Rupin, Anton, Phoenix, Ariz.; Missouri School of Midwifery and Diseases of Women and Children, St. Louis, 1890; practiced in Topeka, Kan.; died July 17, aged 90.

Russell, Murch, Sheridan, Ore.; Ohio Medical University, Columbus, 1905; served on the staff of the McMinnville (Ore.) Hospital; died in Portland July 27, aged 76.

Sabia, Daniel Joseph ✦ Stamford, Conn.; Marquette University School of Medicine, Milwaukee, 1937; member of the American Academy of General Practice; veteran of World War II; on the staff of the Stamford Hospital, where he died Aug. 6, aged 47, of hypernephroma with metastases.

Santoro, Anthony ✦ Chicago; Loyola University School of Medicine, Chicago, 1930; member of the American Academy of General Practice and the Industrial Medical Association; served during World War II; chief surgeon for the Chicago Fire Patrol; on the executive staff, West Suburban Hospital in Oak Park, Ill.; died Aug. 28, aged 58, of coronary thrombosis.

Sarkis, Eleazer Der, Philadelphia; Medico-Chirurgical College of Philadelphia, 1902; an associate member of the American Medical Association; served as Iranian medical missionary; for many years on the staff of the Presbyterian Hospital, where he died Aug. 16, aged 79.

Saunders, Edward Watts ✦ New York City; Washington University School of Medicine, St. Louis, 1924; on the staffs of the Presbyterian and Roosevelt hospitals; died in Edgartown, Mass., Aug. 3, aged 58, of cerebral hemorrhage.

Shafer, Frank Myron, Carthage, Mo.; University Medical College of Kansas City, 1901; served as chief of the medical service at the Veterans Administration Hospital in Fayetteville, Ark., where he died July 16, aged 80, of a cerebrovascular accident with hemiplegia.

Sherman, Elvie Clyde, Cardington, Ohio; Starling Medical College, Columbus, 1896; died July 27, aged 86, of a heart attack.

Shore, John Paul Jones ✦ Sailor Springs, Ill.; Barnes Medical College, St. Louis, 1903; on the staff of the Clay County Hospital in Flora; died July 31, aged 78, of uremia.

Sikes, Gibson L., Raleigh, N. C.; University College of Medicine, Richmond, 1900; member of the Medical Society of the State of North Carolina; died in the Rex Hospital July 25, aged 86.

Simons, Samuel Shirk ✦ Marietta, Pa.; Jefferson Medical College of Philadelphia, 1923; fellow of the American College of Physicians; served on the faculty of his alma mater; associated with the Lancaster (Pa.) General Hospital; died Aug. 2, aged 67, of coronary occlusion and carcinoma of the stomach.

Smith, Lewis Albert ✦ Mansfield, Ohio; Ohio Medical University, Columbus, 1897; on the staff of the Mansfield General Hospital; died in St. Anthony Hospital, Columbus, July 20, aged 83, of arteriosclerotic heart disease and chronic cystitis.

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Spooner, Dostor Sterling, Pahokee, Fla.; Atlanta School of Medicine, 1909; died July 21, aged 76.

Stanton, Frank Everett Sr., Long Beach, Calif.; Rush Medical College, Chicago, 1910; on the staffs of the Long Beach Community Hospital and the Seaside Memorial Hospital, where he died July 29, aged 73, of coronary occlusion.

Stratford, Eldredge Wayne ✙ Portland, Ore.; Harvard Medical School, Boston, 1931; fellow of the International College of Surgeons; veteran of World War II; on the staffs of the Physicians and Surgeons Hospital and the Thomas B. Wilcox Memorial Hospital; died July 25, aged 55, of carcinoma of the abdomen.

Sughrue, Dennis Francis, Boston; Harvard Medical School, Boston, 1898; veteran of the Spanish–American War; died in the Carney Hospital July 29, aged 92, of cerebral thrombosis.

Sullivan, James Aloysius, Jersey City, N. J.; McGill University Faculty of Medicine, Montreal, Que., Canada, 1905; served as chief pediatrician at the Jersey City Medical Center, where he died July 26, aged 75, of cerebral thrombosis.

Swindle, Robert Norris ✙ West Palm Beach, Fla.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1906; member of the Illinois State Medical Society; at one time practiced in Chicago, where he was on the staff of the Roseland Community Hospital; died in the Grant Hospital, Columbus, Ohio, Aug. 17, aged 73, of carcinoma.

Swingle, Alvin Jacob ✙ Benton Harbor, Mich.; Ohio State University College of Medicine, Columbus, 1938; fellow of the American College of Surgeons; veteran of World War II; on the staffs of St. Joseph–Benton Harbor Memorial Hospital in St. Joseph and the Mercy Hospital; died Aug. 1, aged 45, of a coronary attack.

Thompson, Albert Ely, Washington, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1898; an associate member of the American Medical Association; past-president and secretary of the Washington County Medical Society; veteran of World War I; on the staff of the Washington Hospital; fellow of the American College of Surgeons; died July 30, aged 83, of carcinoma of the colon.

Thompson, Penrose Hann ✙ Merchantville, N. J.; Hahnemann Medical College and Hospital of Philadelphia, 1929; member of the American Academy of General Practice; past-president of the Medical Society of New Jersey; for many years on the staff of the West Jersey Hospital in Camden; died in the Memorial Hospital, Somers Point July 24, aged 53, of cerebral hemorrhage.

Van Allen, John Peter, San Antonio, Texas; Kansas City (Mo.) Medical College, 1899; died in the San Antonio State Hospital July 19, aged 80, of acute coronary occlusion.

van Allen, William Roy, Canandaigua, N. Y.; University of Tennessee College of Medicine, Memphis, 1935; member of the American Psychiatric Association; physician in charge, Brigham Hospital; served on the staff of the Florida State Hospital in Chattahoochee; formerly superintendent of the Kentucky State Hospital in Danville; died July 26, aged 57, of coronary disease.

Van Vleet, Mary Elizabeth ✙ Milwaukee; Northwestern University Medical School, Chicago, 1949; certified by the National Board of Medical Examiners; associated with Milwaukee and Columbia hospitals; died July 18, aged 37.

Vonderbeck, John, Louisville, Ky.; University of Louisville Medical Department, 1911; member of the American Academy of General Practice; on the staff of St. Anthony Hospital, where he died July 21, aged 72, of arteriosclerotic heart disease.

Vosburg, Walter Hall, Dunkirk, N. Y.; Cleveland Medical College, Homeopathic, 1897; fellow of the American College of Surgeons; veteran of World War I; member of the city board of health and city council; on the staff of the Brooks Memorial Hospital, where he died Aug. 5, aged 82.

Wakeman, Charles Leonard, Hancock, N. Y.; Eclectic Medical College of the City of New York, 1896; an associate member of the American Medical Association; formerly practiced in Andes; veteran of World War I; served as president of the board and as superintendent of the Hancock Community Hospital; an honorary member of the board of directors of the Read Memorial Hospital, where he died July 4, aged 85, of chronic myocarditis.

White, Homer Evert ✙ Naylor, Mo.; University of Louisville (Ky.) Medical Department, 1909; died July 6, aged 74, of coronary occlusion.

Whitelaw, Henry Neill, Corvallis, Ore.; Rush Medical College, Chicago, 1906; died July 19, aged 82, of cerebral hemorrhage.

Williams, Joseph Murray Jr. ✙ Anthony, Kan.; Temple University School of Medicine, Philadelphia, 1950; served an internship and residency at the Temple University Hospital in Philadelphia; killed July 19, aged 32, when his station wagon overturned.

Workman, Irvin Samuel, Mount Vernon, Ohio; Western Reserve University Medical Department, Cleveland, 1903; died July 6, aged 87, of uremia.

Zimmerman, Fred, Brooklyn; St. Louis University School of Medicine, 1930; died July 19, aged 53, of coronary thrombosis.

FOREIGN LETTERS

BRAZIL

Duodenal Intubation After Cholecystectomy.—Patients who have had a cholecystectomy may be followed up by means of intravenous cholangiography or duodenal intubation. The roentgenmanometric study, by means of laparoscopic cholangiography or through Royer's transhepatic technique requires, in both cases, a previous laborious training. This explains the interest in the study of duodenal intubation as a simpler and more practical method of investigating the postoperative function of the biliary system. Dr. Djalma Vasconcellos (*Hospital, Rio de Janeiro,* **51**:393, 1957) reported a study of 50 patients who had undergone cholecystectomy. Their ages varied between 17 and 67 years; 32 were between 21 and 40. The first 21 were examined before and after operation and the remaining 29 only after the cholecystectomy. After a flow of bile for 15 minutes, a 1% solution of procaine was instilled, and the bile was collected for 15 minutes. The duodenal intubations were performed 1, 6, and 12 months after the operation and in a few patients only after two years. The patients were divided into (1) those who were asymptomatic; (2) those who had hyposthenic dyspeptic symptoms or mild pain; and (3) those who had major symptoms and jaundice. The action of procaine was studied in 31 tests in the patients of the first group. In 27 tests the minute-volume of the bile flow was increased, in three it was decreased, and in one it remained unchanged. In the patients of the second group, 77.7% gave a history of hepatic colic before operation, 11.1% of them with jaundice. In the remaining 22.2%, the postoperative complaints were about the same as before operation. The action of procaine was studied in 17 patients of this second group, in 16 of whom the minute-volume was increased. All the 11 patients of the third group in whom the action of procaine was studied showed an increase in the minute-volume of the flow.

The author concluded that the value of duodenal intubation for the interpretation of the postcholecystectomy syndrome is relative, since the same type of hypertonia is found in a large proportion of asymptomatic patients. It is useful to perform duodenal intubation preoperatively on all patients about to undergo cholecystectomy, as the incidence of functional disturbances occurring preoperatively and postoperatively is about equal. The syndrome of hypertonia of the sphincter of the terminal portion of the common bile duct is frequently observed in patients after cholecystectomy with or without symptoms. In the author's series it was found in 45.4% of the asymptomatic patients—in 64.9% of those with hyposthenic dyspepsia, and in 86.6% of those with painful crises. No case of cholecystectomy syndrome related to sphincteral hypotonicity was observed by the author.

Breech Delivery.—Breech presentation offers the highest rate of difficulties and dangers for the mother, fetus, and obstetrician. Dr. L. R. Rodriguez (*Rev. gynec. obst.* **50**:859, 1957) reported a series of 281 breech presentations in 8,768 deliveries (3.2%). Of the 281 mothers, 146 (51.9%) were primiparas, and their age distribution was as follows: 15 to 19 years, 16; 20 to 29 years, 145; 30 to 39 years, 111; and 40 years or over, 9. There were 42 premature deliveries. There were 30 multiple deliveries (10.6%); a high percentage of mothers of more than 30 years of age (42.7%); a low incidence of maternal deaths (0.3%); a high percentage of mothers needing cesarean section (17.8%), particularly those of more than 30 years (54%); a marked influence of fetus-pelvis disproportion (38%) as the main reason for cesarean section; a higher fetal mortality (56.7%) when the fetus weighed more than 2,500 Gm. (5.5 lb.) than when it weighed less; a high fetal mortality when the mother was over 30, particularly if multiparous (48.6%); and a higher percentage of fetal deaths in spontaneous delivery (81%).

Transfused Erythrocyte Survival.—Dr. Victorio Maspes (*Rev. Hosp. clin.* **12**:208, 1957) reported experimental work which led to a modification of Ashby's method for the determination of the survival of transfused erythrocytes. The necessity of a method of differential serum agglutination that would be accurate and at the same time would not need too much time nor special serums and complicated equipment led the author to undertake this investigation. His theoretical aim was to devise a method as exact as those already described in the literature but, for the performance of which, it would not be necessary to use rabbit serums anti-M and anti-N nor hemolytic and lyophilized serums. He planned to use human serums anti-A and anti-B with high titers to reduce the number of residual erythrocytes. The final result was a modification of Ashby's method, for which the author used dilutions of the order of 0.02 ml. in 1.0 ml. of diluent made with larger volumes than those made with the hematimetric pipets. For the systems ABO and Rh, the serums

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used for the differential agglutination were concentrated by freezing at between −10 C and −32 C with subsequent removal of the supernatant fluid when the serums were thawed. For the systems MN, a powerful phytoagglutinin (a 1:40 extract of seeds of Vicia graminea) was used with advantage for the count, since this extract is a solution in a saline medium and thus has a reduced viscosity. With the use of the Vicia extract, the author obtained results indistinguishable from those obtained with cryoconcentrated serums.

INDIA

Railway Concessions for Patients with Cancer.—Travel concessions granted to blind persons and tuberculous patients were extended to patients with cancer on similar terms starting in July. Patients with cancer traveling alone for admission to or discharge from a hospital need pay only 25% of the normal fare. The patient and an attendant are allowed to travel on payment of one full fare. To obtain this benefit, the patient must present a certificate from the hospital or institute concerned to the effect that the applicant is a bona fide cancer patient traveling for admission to or on discharge from a hospital.

Health Grants.—About $38,000 has been allocated to India by the executive board of the United Nations International Children's Emergency Fund for a program to improve, expand, and integrate the training of physicians in clinical and preventive pediatrics. Under the scheme, eight fellowships, each of one year's duration, would be available in the pediatrics department of the Madras Medical College. The board has also made an allocation of $131,000 for tuberculosis control, $16,500 for goiter control, $383,000 for preschool and school feeding programs, and $1,515,000 for maternal and child welfare services. These amounts are not given in cash to the government, but, when a particular scheme covered by the assistance program develops, supplies and equipment are made available in kind, while the amounts for fellowships and salaries are paid in cash to the institutions concerned.

Amebiasis in Children.—Amebic infection can occur at any age, although it is not as common in children as in adults. A. Bhattacharya and co-workers reported a series of 26 children (18 boys and 8 girls) with this infection (*Bull. Calcutta School Trop. Med.* **5**:2, 1957). Their ages varied from 2½ to 10 years. The duration of intestinal complaints ranged from one to five years. The onset was sudden in 17 patients; 4 had diarrhea alternating with constipation. Other symptoms met with were emaciation, vague abdominal pain, and irregular fever associated with constipation. The liver was palpable in 16 patients. Barium enema examination showed a moth-eaten appearance of a segment of the colon, filling defects, and localized areas of radiolucency. Blood examination revealed anemia and leukocytosis in some patients and a high eosinophil count in others. The sedimentation rate was elevated in four patients. Entamoeba histolytica in the vegetative or the cyst form or both was seen on stool examination in all cases. Ulcers were seen on proctoscopy in eight patients, swabs from these areas being positive for E. histolytica trophozoites. These cases were not diagnosed correctly for some time and were either untreated or treated for bacillary dysentery. The possibility of amebiasis should therefore be considered in children with intestinal complaint and poor general health.

Comparison of Epinephrine, Corticotropin, and Cortisone.—H. G. Roy (*Indian M. Forum* **8**:7 [July] 1957) studied the action of epinephrine hydrochloride, corticotropin, and cortisone acetate on the circulating eosinophil level, on the serum potassium level, and on the ratio of urinary uric acid to creatinine. These drugs produced a fall in the number of circulating eosinophils in normal persons. The count was usually cut in half by the fourth hour after the injection. This depression after injections of epinephrine was transient, corticotropin had a more sustained effect, and the most prolonged action was seen after injections of cortisone. Injections of these drugs caused lowering of the serum potassium level, but the action was not consistent in normal subjects, and the wide fluctuations seen in conditions of stress must be due to some other factor or factors influencing the potassium-ion concentration. The ratio of urinary uric acid to creatinine increased after the injection of all three drugs. This rise was sometimes preceded by an initial fall in the ratio after injections of epinephrine and corticotropin. It reached 100% or more in all subjects after corticotropin and cortisone injection but not after injection of epinephrine. Of the three drugs, cortisone produced the more lasting effect on the ratio, which was maintained at a high level for over three hours after injection. The author concluded that cortisone is the drug of choice for conditions of stress because its effect is more sustained than that of the other drugs. It also acts directly on the tissues and so does not stimulate the hypothalamic-pituitary-adrenocortical mechanism which is already hyperactive in conditions of stress.

Intrapleural Pressure.—N. R. Konar and co-workers (*J. Indian M. A.* **29**:3 [Aug. 1] 1957) studied the changes in intrapleural pressure on the two sides of the chest during inspiration and expiration in normal subjects and in patients suffering from pleurisy with effusion, bronchial asthma, pulmonary emphysema, and cirrhosis of the liver with ascites.

The intrapleural pressure was recorded successively on both sides of the chest at the same sitting. The patients had no analgesics or hypnotics till the investigation was completed. There was significant difference of pressure in the two sides of the chest in normal subjects. The negative pressure was less on the left side than on the right, the difference being about 2 cm. of water. This was true both during inspiration and expiration. In patients with pleural effusion, the negative pressure was less on the affected side, and sometimes a positive pressure was observed. Shifting of the mediastinum to the opposite side caused by the effusion also reduced the negative pressure on the healthy side. During an attack of bronchial asthma, the negative pressure was greater than normal during inspiration and less than normal during expiration. These changes were due to bronchospasm which interfered with normal entry of air into the lungs during inspiration and deflation of the lungs during expiration. In emphysema, the negative pressure was less than normal on both sides during both the phases of respiration due to the diminished elasticity of the distended lungs. In ascites also, the negative pressure was less than normal on both sides during inspiration and expiration due to encroachment of the pleural space by the raised diaphragm.

Tropical Splenomegaly.—Saha and Chaudhari (*Bull. Calcutta School Trop. Med.* **5**:2, 1957) reported a series of 60 patients with tropical splenomegaly in whom the liver was examined by means of a needle biopsy. These patients suffered from irregular fever, and clinical examination showed enlargement of spleen, usually associated with an enlarged liver and hemocytopenia. All of these patients had ascites, five had gastrointestinal hemorrhage, and four had jaundice. Liver biopsy showed normal findings in 14, and 20 had focal necrosis in the liver parenchyma with cellular infiltration and varying degrees of reticular condensation and hyperplasia with proliferation of fibroblasts; diffuse parenchymal degeneration was present in 9 and fatty degeneration in 7. Round cell infiltration in the portal tracts was seen in 41, and 3 had portal cirrhosis. Kupffer's cells were increased in number and size in all the patients. Accumulation of hemosiderin granules in the liver cells and Kupffer's cells was seen in 8 of 20 patients whose specimens were stained for iron pigment. Biopsy was repeated after splenectomy in 8; Kupffer's cells were hyperactive in all of these. One patient whose liver biopsy specimen had shown normal histological findings before operation showed the same postoperatively and was progressing well when last seen. Seven patients who had hepatic involvement before operation were influenced by operation as far as cirrhotic changes were concerned. Four patients who were treated with antimalarial drugs showed reduction in the size of the spleen, but the liver biopsy specimens showed no significant abnormality before or after this treatment. Two patients who did not respond to medical treatment showed progressive involvement of the liver.

Rauwolfia Serpentina and Gastric Acidity.—Rindani and Antia (*Ind. J. M. Sc.* **11**:7 [July] 1957) studied the action of a reserpine-free extract of Rauwolfia serpentina on the free acid content of gastric juice under basal conditions and in response to insulin hypoglycemia. Extracts of R. serpentina from which the reserpine fraction has been removed prevent activation of adrenal cortex during stress in both rats and man without interfering with the action of corticotropin or cortisone in the body, while reserpine itself stimulates the adrenal cortex. It has been suggested by other authors that cortical hormones of the adrenal glands may cause the extravagal stimulation of gastric secretion observed under stress. Insulin hypoglycemia, however, causes gastric hypersecretion by acting on the vagus nerves, presumably by stimulating the hypothalamus. The authors, therefore, decided to study the action on gastric juice of an agent that would inhibit the activation of the adrenal cortex during stress without interfering with the action of corticotropin or cortisone. Samples of gastric contents for assessing basal acidity were collected from 15 subjects, after previous starvation and initial emptying of the stomach, and four further samples were collected after insulin injection in 10 of the subjects. This procedure was repeated after treating them all with a reserpine-free extract of R. serpentina for a day. Part of the drug was given by mouth and part by intramuscular injection. While the drug had no noticeable influence on the basal acidity, there was a significant inhibition of the higher acidity induced by insulin hypoglycemia.

Experimental Viper Venom Poisoning.—R. D. Ganatra and co-workers (*Ind. J. M. Sc.* **11**:7 [July] 1957) stated that the immediate administration of an antivenin is the most useful therapy in patients with snake bite, but it also has its disadvantages. Antihistaminics, corticotropin, and cortisone have been used with antivenin or as the sole form of therapy as an experimental procedure in animals and even in some critical trials. The authors first used hydrocortisone as an adjunct to antivenin and then as the sole form of treatment for snake bite in mice. The dose of antivenin used in these experiments was smaller than that usually used, so that the effect of the supplementary therapy could more readily be evaluated. The LD_{50} for the venom was calculated. Later 2 LD_{50} of the venom and sufficient antivenin to neutralize 1 LD_{50} were injected when the mortality was found to be about 57%. Mortality was reduced to 17% by giving 0.1 mg. of hydrocortisone per gram of body weight

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alone or with antivenin, in spite of the fact that the dose of the venom used was 2 LD_{50}. The beneficial effect of hydrocortisone in poisoning by viper venom may be due to the predominantly hemolytic action of the venom.

Research in Chest Diseases.—A course of training for laboratory technicians was inaugurated in the Vallabhbhai Patel Chest Institute, Delhi, in July. This should make possible a fuller use of the institute's laboratory. Two experts from the United States are helping to organize this course. The main function of the institute is research in diseases of the chest and training of chest physicians. The institute has so far conducted investigations on the effect of antituberculosis drugs; the determination of circulation time in human beings and animals with use of radioactive isotopes; an inquiry into infectious hepatitis; and identification of certain nerve receptors in the heart, lungs, and stomach.

NEW ZEALAND

Asian Influenza.—The Influenza Advisory Committee announced that the department of health will continue to watch closely developments relating to Asian influenza. The committee, led by the director-general of health, is comprised of prominent practitioners and senior health officers. All available evidence indicates that the current epidemic is of a mild type and extremely prevalent, especially among children. It must be recognized, however, that in any influenza epidemic, no matter how mild, and regardless of the strain, a few deaths may occur. Recent reports from Australia suggested some new association of Micrococcus pyogenes var. aureus resulting in lung complications. The committee emphasizes, however, that such complications can and do occur in the absence of influenza. The deaths from lung complications that have occurred to date conform to this well-known pattern and in no way invalidate the view that the current influenza epidemic is one with a high morbidity and a low death rate. No deaths due to uncomplicated influenza have occurred. The symptoms of the disease are easily recognized. The disease has a rapid onset with headaches, dizziness, cough, and fever. The temperature falls in two or three days and sometimes rises again on the fourth or fifth day. Recovery occurs in about one week. Since there is no specific treatment for the disease, victims should stay in bed until their temperature has subsided. Bed rest is the essential feature of the treatment, and if the condition does not clear up in two days the family physician should be consulted. As long as influenza is epidemic in any particular locality, the young should avoid vigorous exercise and competitive sports should be interrupted.

In Auckland hospitals, 51 patients with pneumonia were admitted in four days (Aug. 23 to 27). Although the superintendent of the hospital board was not able to say definitely whether the Asian influenza virus was responsible for these cases, there was strong suspicion that this was the case. A special ward will be opened at Green Lane Hospital to receive patients suffering from complications of influenza, should the number increase. This would be manned by the permanent staff whose normal duties would be performed by a temporary staff. Three young children believed to have been suffering from Asian influenza died in Wellington. In a 15-month-old infant, death occurred within 12 hours. A 16-year-old boy who arrived with his schoolmates at a holiday camp suddenly became dyspneic. He was taken to a hospital where he died three hours later of pneumonia.

People who wish to obtain vaccine against Asian influenza can do so through their family physicians. Because the vaccine was made by a private firm in Wellington, it could not be supplied free of charge. Vaccine used for hospital staffs and others in the "special risk" group came to the health department from the Commonwealth Serum Laboratories in Australia, but there was not enough of this to supply even this limited demand. The press has accused the Influenza Advisory Committee of unwarranted complacency. In September the epidemic was sweeping through North Island centers and was expected to bring with it a serious loss in production. Some editorials have opposed the decision of the committee that there is no justification for general community inoculation against influenza in view of the mildness of the disease. The epidemic is having repercussions on the social life too. In Gisborne a singing contest was discontinued when the judges became ill. Because 8 of 76 boys in a holiday camp at Reikorangi, Waikane, were affected by influenza, it was decided to disperse the Wellington boys to their homes to avoid the possibility that the whole camp would be affected. The 40 or so boys from the South Pacific Islands who are in New Zealand under the direction of the Department of Island Territories will remain in camp, as they are attending boarding schools.

Influenza has seriously affected the physical fitness of the Fijian football team at present on a tour in New Zealand. Members of the Invercargill Borstall staff are playing the part of nurses to about 100 inmates of a total of 209 confined to bed with influenza. The epidemic first struck the institution one Sunday, and two days later the number of victims had grown to 100. In order not to alarm the citizens, the press has tended to minimize the state of the epidemic. In Dunedin its morbidity is now serious; the staffs of all city shops, hotels, and hospitals are almost depleted. At the Otago Medical School the work at the experimental animal headquarters is carried out by school children who volunteered to

cope with the emergency. A druggist in Wairarapa reported a sharp rise in the sales of smelling salts, usually in very low demand. In Wellington people have bought out available supplies of ammoniated quinine believing it to be a sure cure. Perhaps, in Dunedin, the most popular cure is aspirin with lemon or hot whisky.

NORWAY

Courtesy to the Relatives of Dying Patients.—Dr. Karl Evang has issued an appeal in the organ of the Norwegian Medical Association to his colleagues in general and the staffs of hospitals in particular with regard to near relatives of patients whose deaths in the hospital are associated with painful circumstances aggravated by carelessness on the part of physicians or nurses. By virtue of his position, he has to deal with complaints of this kind. In certain cases, rare and exceptional though they are, physicians and nurses may leave the impression on the minds of the relatives that enough has not been done to save life or, at any rate, relieve suffering. Hospital physicians have been held to have been dilatory in their attendance during the last phases of the patient's illness and to have lacked consideration when speaking to his relatives after his death. A complainant may force his way to the hospital head who has hitherto been unable or unwilling to give him an audience. By now the complainant may have become more suspicious than ever, and the head is on the defensive, scenting trouble with claims for compensation. Deaths among the young and the middle-aged have now become so relatively rare that many people are tempted to assume that some blunder must be responsible when they do occur. There has also been a change in the attitude of the public to physicians whose authority is no longer what it was. Clear and detailed explanations are now required of them, and they must not talk down to people or put them off as incapable of understanding medical matters. Evang's advice to the heads of hospitals is to take up this subject with the staffs and to impress on them how to meet halfway the sorrowing relatives of the dying.

Dermatitis from Creaseless Fabrics.—A recent case of dermatitis due to clothing and treated at the skin department of the Rikshospital in Oslo has led to a systematic study of creaseless fabrics rendered such by treatment with formaldehyde or formalin. Traces of it are apt to linger in the material thus treated. On the assumption that formalin might be responsible for creaseless fabric dermatitis, the first step taken was to apply standard epicutaneous skin tests to 110 consecutive persons (66 men and 44 women) suffering from idiosyncratic eczema. Among them were 13 men and 11 women giving a reaction to formalin. These 24 patients were tested with one or another of the seven different creaseless fabrics available for testing. The fabrics were moistened with water, and the patient reactions were read 48 and 72 hours later. After 72 hours there was a definite reaction in four women and one man. Five men and five women who did not suffer from eczema were also tested in the same way with some creaseless fabric, but in none of these was any reaction provoked. Three of the four women reacting to some creaseless fabric had a history and clinical findings of "dress dermatitis." Dr. Oddvar Andrup, (*Tidsskrift for den norske lægeforening*, Aug. 15, 1957) draws attention to the rapid development of textiles treated with resins to confer certain properties on them and to the need for special marking of such textiles so that persons liable to formalin dermatitis may be forewarned.

Surgical Treatment of Lumbago-Sciatica.—Dr. K. Kristiansen (*Nordisk medicin*, Aug. 8, 1957) reported a series of 177 patients who had been operated on for lumbosacral herniation of the nucleus pulposus. This involved the fourth intervertebral disk in 104 cases. The cases were, on the whole, severe, and they included 27 in which the bladder or rectum was paretic. Myelography with a water-soluble iodine contrast medium was carried out in every case and with positive findings. The operation was performed with the patient in the knee-elbow position, and osteofixation of the spine was performed according to the Smith-Petersen technique after removal of the herniation. The patients were allowed out of bed on the day after the operation and discharged from hospital on the 14th to 16th postoperative day. There were no postoperative deaths, and the thrombosis-embolism rate was 15%. Though Kristiansen admitted that there was still disagreement throughout the world over the merits of spondylofixation as a supplement to removal of the herniation, he was so pleased with the results of the combined operation that he still adhered to it, having found that the herniation is but part of the trouble which is associated with osteochondrosis and changes in the intervertebral joints. His assistant, Dr. Nils Eie, undertook a follow-up examination of 113 of his patients with an observation period of one to six years after the operation. He found 110 to be fully fit for work and 101 entirely free from pain. Of the three patients who relapsed, two did so on heavy work after having been perfectly fit for work after the first operation. All three were operated on again, and two of them became free of pain.

Leukemia After Radiotherapy.—Recently the staff of the Aalesund City Hospital was struck by the frequency with which the patients admitted for leukemia gave a history of radiotherapy at some earlier date. To throw more light on this point, Voll and Tveit (*Nordisk medicin*, Aug. 1, 1957) searched the records of this hospital for the period 1950-1956 and found that 31 patients had been treated in it for

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leukemia. Among them were 10 who had previously been treated with radium or x-ray for various ailments and periods. Six of the 10 had received relatively large x-ray doses which had, however, been spread over several years. All 10 patients suffered from acute leukemia or chronic granulocytic leukemia—not one from chronic lymphocytic leukemia. Other observers have also noted the absence of cases of chronic lymphocytic leukemia in association with previous radiotherapy. If no causal relationship exists, one might expect all the different forms of leukemia to be represented now and then in association with radiotherapy.

UNITED KINGDOM

The Welfare State.—At the end of 1956, the Ministry of Pensions and National Insurance was paying nearly 840,000 war pensions, about 3,500,000 family allowances, 4,500,000 retirement pensions, 470,000 widows' benefits and guardians' allowances, and 140,000 industrial disablement pensions. Over 257 million dollars was paid in war pensions during the year, an increase of about 28 million dollars over the previous year. Of the 840,000 war pensions, 364,000 were for World War I and 476,000 for World War II. The total of 840,000 includes 601,000 disability pensions, 158,000 widows' pensions, and 80,000 pensions for parents, orphans, and other dependants. New claims for sickness benefit in 1956 totaled 7,750,000 at a cost of nearly 280 million dollars. It is estimated that 770,000 maternity benefits, 295,000 home confinement grants, and 164,000 maternity allowances were paid during the year, at a cost of 39 million dollars. The combined cost of these and other benefits paid by the ministry was at the rate of nearly 2.5 billion dollars a year as of Dec. 31, 1956.

Sodium Bicarbonate Intoxication.—Two cases of sodium bicarbonate intoxication are reported by A. G. Melrose (*Scottish M. J.* **2**:301, 1957). The first was that of a simple-minded young man of 21, who was advised by a relative to take sodium bicarbonate for indigestion. He promptly swallowed 1 lb. of the salt. Violent tetanic spasms ensued, and the man died in coma two hours later before effective medical aid could be given. The other case was that of a male nurse, aged 56 years, who at the age of 29 had been told by a physician to take sodium bicarbonate for indigestion, and who had consumed 2 lb. weekly over a period of 27 years. When seen at the age of 56, he was found to have alkalosis, with some impairment of renal function. He reacted violently to the withdrawal of sodium bicarbonate when he was admitted to hospital—so much so, that small doses had to be reinstituted and then gradually withdrawn. Apparently, the patient consumed sodium bicarbonate largely because the distension of the stomach and subsequent eructation gave rise to pleasurable sensations.

Hemophilus Influenzae.—A marked increase of H. influenzae in throat-swab cultures was reported by David Harley (*Lancet* **2**:191, 1957). The patients concerned were allergic subjects in whom a routine bacteriological survey of the upper respiratory tract was carried out, and, with one exception, none of them gave a history of any recent acute febrile respiratory illness. The organism occurred in a heavy growth as the predominating or only organism in the pathogen-selective culture. At exactly the same time of the year in 1918, the late John Matthews reported finding H. influenzae in cultures—just prior to the epidemic outbreak of influenza in 1918.

Diphtheria and Pertussis Immunization.—The Ministry of Health decided to discontinue supplies of alum-precipitated toxoids (APT) and to issue only fluid or formol diphtheria toxoid (FT) and diphtheria toxoid antitoxin floccules (TAF). It is recommended that the primary course of immunization should consist of two injections each of 1 ml. of FT at a minimum interval of 28 days and that a single injection of 1 ml. be used for booster doses. TAF is recommended in a 1-ml. dose for the booster in children over 5 years of age who have been primarily immunized with APT, PTAP, or combined diphtheria-pertussis vaccine and who may, in consequence, be unduly sensitive to FT. There is no change in the advice that immunization against diphtheria should take place at about 8 or 9 months of age, so that protection can be completed before the first birthday, with a booster dose in the fifth or sixth years. The Minister of Health is now satisfied that an effective plain pertussis vaccine can be produced, and he urges all local health authorities to offer immunization against pertussis as part of their arrangements. It is recommended that the first injection be given to children at not later than 3 months of age. On the subject of combined antigens, the Minister sits firmly on the traditional fence. Supplies of combined antigens have not been issued to local health authorities, but most authorities have proposals approved by the Minister which enable them to make arrangements for combined immunization against diphtheria and whooping cough and sometimes also tetanus. It is not possible, without further knowledge, to give any guidance on the use of tetanus antigens in combination with diphtheria or whooping cough antigens.

Influenza, 1953-1956.—In a report from the Public Health Laboratory Service (*Brit. M. J.* **2**:8, 1957) on the incidence of influenza from 1953 to 1956, it is stated that morbidity and mortality statistics taken in conjunction with laboratory results suggest that no severe epidemic of influenza occurred in the

three winters, 1953-1956, although influenza B was prevalent in most parts of the country during the winter of 1954-1955 and influenza A during the winter of 1955-1956. Localized outbreaks and sporadic cases of influenza A were detected fairly often in the first half of 1954 and the first half of 1955. Sporadic cases and small outbreaks of virus B infection were detected in the late winter of 1953-1954 and less often since the large epidemic that followed. Most of the virus A infections in the period were probably due to a virus of the Scandinavian group. Infections associated with Eire '55 and Dutch '56 viruses occurred but were much less prevalent. Influenza virus B strains isolated in the 1954-1955 epidemic differed antigenically from earlier strains of this group. The frequency with which respiratory illnesses associated with influenza A and B infections were detected between epidemics was compatible with the hypothesis that both diseases are endemic in this country.

Salmonella in Fertilizers.—Fertilizers from human and animal sources are widely used in agriculture and horticulture. Practically all farmlands and many gardens are treated with such fertilizers. Fertilizers of human origin are mainly products from sewage-works, cesspits, and septic tanks, while those of animal origin are mainly blood, bone, horn, and hoof, or derived from fish. Sludge from septic tanks and cesspits is usually spread on the land in the crude state, and that from sewage works is generally processed. It is well known that sewage and sludge may contain pathogens, especially Salmonella. Fertilizers of animal origin come from glue factories or factories specializing in the manufacture of fertilizers, and some are imported. Walker (*Lancet* **2**:283, 1957) examined a large number of organic fertilizers and found many of them infected with Salmonella of various types. Such organisms were present in 70% of the bone meal samples, 54% of the samples of dried sludge, 33% of the hoof and horn samples, and 15% of the dried blood samples. The anthrax bacillus was also isolated from all these sources. Walker suggests that organic fertilizers may be a source of infection of vegetables and animals and thus, ultimately, of man. Three of the types most often isolated from the fertilizers were high on the list of Salmonella isolated from human beings. When outbreaks of Salmonella infection are investigated, organic fertilizers have never been considered as a possible source of the organisms. Bone meal is used more than any other fertilizer and is incorporated in many animal feeding stuffs. It could be a serious source of infection.

Antihemophilic Globulin.—The abnormal bleeding of hemophilia is due to the hereditary deficiency of a normal clotting factor called antihemophilic globulin (AHG). The minimum blood level of AHG compatible with effective hemostasis is about 30% of the average normal. As levels fall below this figure, the tendency to bleed becomes progressively greater, until, in severe grades of hemophilia, AHG is virtually absent. It is difficult to raise the blood AHG level to 30% by giving blood or plasma because of the large volume required and because half the AHG is destroyed in 4 to 11 hours. Human blood is unlikely to be a practical source of AHG, as the number of permanent donors required to supply the hemophiliacs in Britain is estimated to be 500,000. Work is proceeding at Oxford University on the extraction of AHG from ox or pig blood. The most active material so far obtained has an activity of about 8,000 times that of the same weight of fresh human plasma. Macfarlane and co-workers described the use of AHG from bovine or pig blood in 22 hemophilic patients undergoing operation or dental extraction (*Lancet* **2**:251, 1957). The average dose of 200 to 400 mg. was equivalent in activity to about 2,500 ml. of fresh human plasma. In no case was there abnormal bleeding while the level of AHG was above 30% of normal. In the cases of clean wounds, the temporary raising of the AHG level by one or two injections was followed by complete healing without hemorrhage. In all cases, healing was rapid during AHG treatment.

The AHG used is probably antigenic, since, after 10 to 14 days' treatment with bovine or pig AHG, mild allergic reactions may occur after each injection. The antigenicity is probably low because, in the patients treated, skin tests remained negative and no antibodies or anticoagulants active against the AHG could be demonstrated in the patients' blood. There may be a transitory fall in the platelet count after the injection of bovine material. The allergic reactions occurring after 10 to 14 days' treatment were adequately controlled by antihistaminics. No adverse after-effects were observed in any of the patients. Animal AHG proved lifesaving in at least three patients. Like antitoxins and other serums, AHG as now used is potentially dangerous. The risk of anaphylaxis contraindicates a second course of the same preparation in the same patient. Animal AHG should not be used unless the patient's life is in danger, because once it is given the patient is deprived of a treatment that might be required in some future emergency. In patients with mild hemophilia, the rapid transfusion of large volumes of human plasma permits major and minor surgical operations without excessive bleeding.

Poisoning in Children.—"Prescriber's Notes," a circular sent to physicians by the Ministry of Health, refers to the growing number of fatal cases of poisoning in young children due to swallowing medicinal tablets. At present, half the deaths from poisoning in children are due to this cause, the commonest substances being ferrous sulfate, antihistaminics, and aspirin. The circular states that the only effective way of preventing deaths of this sort is to persuade

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parents to keep all medicines out of the reach of children at all times. Practitioners can help by continuing to urge their patients to see that this is done and by calling attention, when visiting homes, to any medicines they may see lying about.

Medicine in Russia.—Dr. R. S. Saxton (*British Medical Journal*, supplement page 95, Aug. 17, 1957) states that 70% of the physicians in Russia are women. Towns are divided into districts or sections, each of which is served by a polyclinic staffed by physicians corresponding to general practitioners and by "specialists" whose status corresponds to that of a hospital resident. The polyclinic varies in size and function according to the size and needs of the population it serves. Thus, in industrial areas, there may be one for children staffed by pediatricians and one or more for adults. These may overlap in the service offered, so that the adults of the family of a factory worker might attend the factory polyclinic. Polyclinics, far distant from hospitals, might serve a population of about 70,000 people living within a radius of one and one-half miles. A large one may be staffed by as many as 90 physicians. They work six hours a day, and their pay varies from that of the director at 1,700 rubles a month to a "specialist" at 930 rubles and a section physician at 800 rubles. Those in the higher ranks, such as professors, earn much more. Attempts to convert these figures into Western currency values would be meaningless, but 800 rubels a month equals the wages of a skilled worker in industry working an eight-hour day. Physicians are permitted to do extra part-time work and to engage in private practice.

The polyclinics are well equipped with numerous consulting rooms, radiological and physiotherapy departments, an operating room, antenatal clinic, and a number of small wards containing 50 beds in some of the larger buildings. The ambulant patient may call and make an immediate appointment if the condition is urgent. On an average, the section physician sees five and the "specialist" eight patients an hour. Patients may decide that they need special treatment and bypass the section physician. Consultations and examinations are friendly and orthodox according to British standards. After examination, the physician may write a prescription, send the patient for radiological or laboratory investigations or for special forms of treatment, refer the case to a specialist for advice, or admit the patient to one of the polyclinic beds. The polyclinic thus functions as a small hospital. Incapacity certificates can be given for a week. Periods longer than this must be certified by medical referees. After the patient has been incapacitated for six months, a district medical commission reviews the case.

House calls are made if the patient is unable to attend the polyclinic. The visiting physician has usually five or six such calls a day with three hours to do them in, a car and chauffeur being provided. For urgent cases, emergency doctors are on call. In about 10 to 12% of the house calls, a specialist is called in. Drugs and treatment are similar to those used in England, although a number of obsolete preparations and methods are still in use. Thus, dry cupping is still used, leeches are applied to the mastoid region for the treatment of hypertension, and intramuscular injections of magnesium sulfate are given. The more expensive drugs are free and are prescribed by the physicians. Other drugs are available fairly cheaply and at state drug stores.

Emphasis is placed on prevention. All physicians are expected to spend four hours a month in health education. Suitable patients from the polyclinics are sent to sanitariums or rest homes. Efforts are made to give all workers an annual medical check up. With a population of nearly 200 million and doctors working six hours a day or less, it is difficult to see how this can be done effectively. Women are encouraged to visit a gynecologist three times a year with a view to detecting precancerous conditions. Physicians in Russia are urged to keep up to date. There is a weekly clinicopathological conference at the polyclinics, and every three months section physicians have a tour of duty in the wards, so that they can have further experience of treating inpatients. Surgeons spend a third of the year working in hospitals. Physicians in Russia have a comparatively easy time. Outside their six hours a day they are free of responsibility. Secretarial assistance, nurses, office accommodation, instruments, apparatus, transportation, and, in fact, everything are provided by the state.

Combined Corticosteroid and Aspirin.—Tablets containing 0.5 mg. of prednisolone or prednisone and 0.3 Gm. of aspirin are now commercially available, although existing evidence does not support the view that the therapeutic effect of corticosteroids is enhanced by the simultaneous administration of aspirin, or vice versa. The recommended maximum daily dose of these compound tablets represents a full dose of aspirin (4 Gm.) but a dose of prednisolone (6 mg.) that is usually ineffective in rheumatoid arthritis. It is difficult to see how a formulation of this kind can be of use in the treatment of rheumatic diseases responding to prednisone or in rheumatic diseases for which aspirin is prescribed but for which prednisolone is not indicated.

Hazards in Diagnostic Radiography.—Dr. W. G. Clarke (*Lancet* **2**:316, 1957) stated that much unnecessary exposure occurs in diagnostic radiography, even of the chest. During investigations into the dose of radiation to the skin and gonads in a number of radiographic units, he observed that patients often receive unnecessary radiation when standard cones are used. The standard 2.5-in. circular diaphragm in common use gives a gonadal exposure of

0.7 mr. The dose of extraneous radiation in chest radiography can be greatly reduced by inserting a sheet of lead 1 mm. thick with a 1.5-in. square hole in its center at the base of the cone. This reduces the gonadal radiation in men to 0.1 mr, or one-seventh of that received when the standard 2.5-in. circular diaphragm is used. This still gives an adequate chest exposure.

Misuse of Antibiotics.—The Ministry of Health warns against the indiscriminate use of antibiotics. It quotes Jawetz's statement that in the United States only 1 to 5% of the antibiotics and sulfonamides administered are given on proper clinical indications. The ministry states that in Great Britain far too many patients are still exposed to the unpleasant side-effects and occasional dangers to which all antibiotics may give rise. A disservice is done to the community as a whole when organisms are made resistant as a result of the unnecessary administration of these drugs. The ministry further states that antibiotics are rarely needed by afebrile patients and that if a patient is ill enough to receive an antibiotic he is usually ill enough to be in bed. Broad-spectrum antibiotics with their potential unpleasant side-effects are often used instead of penicillin when penicillin would be a better choice. Treatment is far too often continued in the absence of a clinical response, and, even when there is a response, an antibiotic is often given over too long a period. The physician who shows some restraint and who makes penicillin his first choice is likely to do more good and is certain to do less harm than he who prescribes antibiotics indiscriminately.

CORRESPONDENCE

TICK PARALYSIS

To the Editor:—Although more than 360 cases of tick paralysis have been reported in the United States since 1912, this possibility may be overlooked. Prompt recognition and early removal of the tick results in a cure of this bilateral symmetrical ascending motor paralysis. No other neurotoxic disease responds as quickly and as completely. A 2-year-old girl was admitted to the University Hospital, Augusta, Ga., at 2:10 p. m. on April 29. She had attended a picnic on the preceding day where she played in a brushy area. The child was very active and playful until 9 p. m. At that time her mother noted that she was not walking normally. The next morning the child could not get out of bed. She also complained that her mouth hurt. She was seen promptly by her physician who examined her and advised observation for two hours. In less than two hours, the mother noticed that the child's arms were weak and that she could not hold her head erect. The physician then advised hospitalization. She was admitted with a tentative diagnosis of poliomyelitis. She had no fever but her pulse rate was 140. On admission she was in no acute distress. Her sensorium was clear, although it was noted that she occasionally had brief periods of wide-eyed staring. There was a generalized flaccidity of her arms and legs, but she could move her arms and hands a little. Her respiration was slightly accelerated and abdominocostal in type. She had some difficulty in swallowing, but no regurgitation. Her knee-jerks and ankle-jerks were absent bilaterally. Her abdominal reflexes were present but sluggish. Laboratory tests including a lumbar puncture were essentially normal. A search for a tick was made and at 6:30 p. m. a female Dermacentor variabilis was found in the occipital region. It was removed by the use of ether and gentle traction. The hypostome was intact. Five hours later there was slight improvement in the patient's muscular power. At this time, 100 mg. of hydrocortisone was given intravenously. Six hours later a second dose was given. Fourteen hours after the tick was removed the child could pull herself up in her crib and 25 hours after the tick was removed, she was capable of normal activity.

One unusual aspect of this case was the short period of time from attachment of the tick to the onset of paralysis. Several investigators have said that the gravid female tick must be attached for a period of five to eight days before causing paralysis. This child became paralyzed about 18 hours after the tick made contact with her body. Prior to April 28 she had not been in an area known to be infested with ticks. Also, the tick was small and relatively unengorged, measuring 4 by 7 mm. To account for the early onset of paralysis in this case it must be assumed that the tick had fed on another human being or other animal shortly before attaching to the child or that it is not always necessary for the tick to feed for several days before transmitting its neurotoxin. Another interesting aspect of this case was the use of corticosteroids. There are no reports of the use of corticosteroids in tick paralysis. Because of the rapid progression of the paralysis and in view of the child's early swallowing difficulty corticosteroids were given, admittedly on an empirical basis. Comparison of this case with experience with other patients indicates that hydrocortisone in the amount given neither hastened nor retarded recovery from the paralysis.

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MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Hemorrhagic Pericarditis, Pleurisy, and Pneumonia Complicating Recent Myocardial Infarction. H. Dressler, J. Yurkofsky and M. C. Starr. Am. Heart J. **54**:42-49 (July) 1957 [St. Louis].

Recent myocardial infarction was complicated by intensely hemorrhagic pericarditis, pleurisy, and pneumonia, respectively, in 3 men between the ages of 52 and 59 years. Pain of the pericardial type and congestive heart failure occurred 6 weeks after myocardial infarction in the first patient. Eleven weeks after onset of the coronary infarction, symptoms and signs of pericardial effusion were noted. Pericardial paracentesis revealed intensely bloody fluid and was followed by rapid improvement. Cultures of blood and aspiration fluid yielded no growth. The patient had not received anticoagulant therapy. Myocardial infarction was accompanied by an unusually prolonged febrile period in the second patient. A loud pericardial friction rub that was audible for 10 days, electrocardiographic changes, and enlargement of the cardiac shadow in the roentgenogram supported a diagnosis of pericarditis with effusion. Signs of bilateral pleural effusion became manifest on the 13th day of illness. Thoracentesis yielded bloody fluid. There were none of the usual indications of pulmonary infarction. Anticoagulant therapy was used for 6 days only. The prothrombin time never exceeded therapeutic levels and had returned to normal 3 days before hemorrhagic pleural effusion became manifest. Acute myocardial infarction was complicated by pericarditis, pneumonitis, and pleurisy in the third patient. Hemorrhagic pneumonia was the predominating complication. It developed on the third day of illness and spread rapidly, involving both lungs. No responsible micro-organism was discovered. Antibiotics were of no avail. Improvement followed administration of cortisone. Treatment with bishydroxycoumarin (Dicumarol) was given initially and was discontinued after 4 days. The prothrombin time was on 2 days only above 30 seconds, the maximum being 36 seconds. The pulmonary process lasted for about 4 weeks.

The cases of these 3 patients and similar ones reported in the literature under the heading of hemopericardium complicating myocardial infarction presented features such as were described recently as characteristic of a post-myocardial-infarction syndrome (*J. A. M. A.* **160**:1379 [April 21] 1956). Among the significant features of the post-myocardial-infarction syndrome a tendency to hemorrhagic inflammation should be included. The fact that anticoagulant therapy was not used in the case of the first patient with hemorrhagic pericarditis and was employed for only a few days in the other patients, the prothrombin time not exceeding therapeutic levels, indicates the necessity to consider other causative factors, besides anticoagulant therapy, responsible for hemorrhagic complications of myocardial infarction.

A New Syndrome of Parotitis with Herpangina Caused by the Coxsackie Virus. J. G. Howlett, F. Somlo and F. Kalz. Canad. M. A. J. **77**:5-7 (July 1) 1957 [Toronto].

The Coxsackie virus, first isolated and described by Dalldorf and Sickles in 1948, has been isolated with regularity from patients with herpangina, pleurodynia, short summer pyrexias, and aseptic meningitis. Clinically, herpangina is characterized by greyish-white papulovesicular lesions of 1 to 2 mm. in diameter with erythematous bases located on the anterior pillars, soft palate, and tongue. This particular disorder occurs in small children during the summer in small epidemics and is further characterized by a sudden onset of fever with accompanying sore throat, dysphagia, anorexia, occasional abdominal pain, and headache. The fever usually persists for 2 or 3 days and the lesions 4 to 6 days. Four cases of parotitis associated with vesicular lesions on the oral mucous membrane from which Coxsackie virus (group A) has been isolated are reported. No increase in antibody titer in any of the samples for mumps and herpes simplex virus was found during the convalesence period, nor was any found in the initial samples. All 4 patients were shown to have Coxsackie virus in the saliva, and in 2 of the 4 the virus was found in the stool. In 2 additional cases resembling herpangina, Coxsackie virus could not be demonstrated.

The place of publication of the periodicals appears in brackets preceding each abstract.

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Aortic Arch Syndromes: A Survey of 5 Cases. J. Burstein, B. Lindström and C. Wasastjerna. Acta med. scandinav. **157**:365-378 (No. 5) 1957 (In English) [Stockholm].

The authors report on 3 women and 2 men with the aortic arch syndrome. The first patient, a 56-year-old woman, had been operated on twice for tumors of the ovaries, and the ovaries were destroyed by radiation when the patient was 41. Myocardial infarction occurred when she was 43 and 47. When she was 50, an ulcer occurred in the nasal septum which extended gradually, and the whole nose became necrotic. Somewhat later she suddenly became blind in one eye, and in the following year the vision of the other eye was greatly weakened. She was admitted to hospital because of attacks of giddiness and anginal pain. Arteriography revealed obliteration of the left subclavian artery, distal narrowing of the left common carotid artery, and obliteration of the left external carotid artery at its base. Intensive treatment with corticotropin and prednisone was ineffective, but distinct improvement by epithelization of the facial ulcer was obtained with anticoagulant therapy and treatment with beta-pyridyl carbinol. The patient had almost all the symptoms which Ross and McKusick observed in patients with aortic arch syndrome. The removal of the ovaries must have favored the development of atheromatosis. Her coronary attacks were most likely caused by severe coronary atheromatosis. The ineffectiveness of steroid therapy also pointed to atheromatosis. An atheromatous aortic arch syndrome seemed to be most likely in this patient.

The second patient, a 31-year-old woman, had had attacks of fainting since her adolescence. In the past 6 years her fingers had occasionally turned white without any reason; she had migraine-like headaches accompanied by disturbances of the visual field, and in the past year she had had a myocardial infarction. Arteriography revealed obliteration of the left subclavian artery. The possibility of atheromatosis as the causative factor in the aortic arch syndrome in this patient was supported by hereditary tendencies, hypoplasia of the sex organs (the appearance of angina pectoris in connection with nonappearance of menstruation), and lack of genuine rheumatic infection, lack of tachycardia, and increased sedimentation rate. The third patient, a 27-year-old woman, had repeated attacks of sore throat in her childhood. At the age of 13 she had rheumatic disease of the joints. Her erythrocyte sedimentation rate was constantly increased, she had persistent tachycardia, her left arm tired rapidly, and she had attacks of giddiness. Obliteration of the left subclavian artery was revealed by arteriography. The aortic arch syndrome in this patient was caused by the rheumatic disease. In the 4th patient, a 51-year-old man, with numbness and subnormal blood pressure in the left arm, degenerative damage in the retina, and intermittent claudication in the legs, the aortic arch syndrome was probably caused by atheromatosis, with which the patient's age and sex were consistent. The severe circulatory disturbances in the legs and the high cholesterol level in the blood also favored the assumption of atheromatosis. In the 5th patient, a 56-year-old man, whose condition was completely dominated by obliterative processes in the lower extremities, examination revealed pulselessness of the right radial artery and of the cubital, axillary, and carotid arteries. The femoral arteries were pulseless on both sides. This psycholabile patient left the hospital before arteriography could be performed. Of the 3 causative factors of the aortic arch syndrome, namely, atheromatosis, thromboangitis obliterans, or syphilis, the first one seemed most probable.

The authors believe that atheromatosis is a far more common causative factor than the available literature shows. It seems noteworthy that in the first 2 patients the course of the disease was dominated by coronary symptoms and myocardial infarctions which, in all probability, were caused by the basic vascular disease producing the aortic arch syndrome. While administration of corticotropin, cortisone, and antibiotics should not be considered in the treatment of the aortic arch syndrome of atheromatous origin, the administration of anticoagulants seems to be beneficial.

Gastric Ulcer and the ABO Blood-Groups. R. H. Balme and D. Jennings. Lancet **1**:1219-1220 (June 15) [London].

On the basis of the assumption (1) that patients with carcinoma of the stomach are more likely to belong to blood group A and those with duodenal ulcers to group O than are controls and (2) that patients with gastric ulcers come somewhere in between, it had been suggested as an explanation that blood group A was associated with a tendency for the mucosa of the body of the stomach to atrophy and that the atrophic mucosa and consequent hypochlorhydria produced a lessened liability to duodenal ulcers and an increased liability to carcinoma. The authors tested this hypothesis by investigating whether blood group A was in fact associated with carcinoma of the body rather than with carcinoma of the antrum. They could do this because in a series of cases of relatively early carcinoma they had already determined the probable site of origin. Contrary to what the hypothesis demanded, there was an excess of group O patients among those with carcinomas of the body and of group A patients among those with carcinomas of the antrum. These results being only on the borderline of statistical significance, they were not reported until further study showed that simple gastric

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ulcers behaved in a similar way, i. e., simple ulcers of the antrum tended to be associated with blood group A, whereas the common gastric ulcer just above the angulus was associated with blood group O.

The authors were able to classify with regard to the site of the gastric lesion and the sex and blood group of 192 patients with gastric ulcers and 119 with carcinoma of the stomach. They found that blood group A predominated when the lesion was in the pyloric antrum and blood group O when it was in the body of the stomach. They believe that the association between gastric carcinoma and blood group A on the one hand and between gastric ulcer and blood group O on the other may be attributable to the fact that most carcinomas are in the antrum, whereas most gastric ulcers are in the body of the stomach.

Increasing Prevalence of Unexplained Liver Necrosis. J. G. Brunson, P. L. Eckman and J. B. Campbell. New England J. Med. **257**:52-56 (July 11) 1957 [Boston].

A review of current autopsy material from the University Hospitals in Minneapolis revealed what appeared to be an increase in the prevalence of unexplained liver necrosis. To evaluate this impression, 3,229 autopsy protocols of patients examined at the University Hospitals morgue from 1946 through 1955 were reviewed and analyzed for gross and microscopic evidence of liver necrosis. In the preliminary survey, every case of liver necrosis was included, and the microscopic slides examined. After this examination, and in conjunction with a study of the clinical and autopsy records, the following cases were excluded: eclampsia; focal central necrosis of the liver associated with shock, cardiac failure, or both; the necrosis that may be associated with cirrhosis; "subacute yellow atrophy"; the necrosis associated with intrahepatic neoplasms; cases of scattered focal areas of hepatic necrosis associated with gram-negative bacteremia and shock; the necrosis associated with chemical poisons; the necrosis associated with abscess formation; and the cases of ischemic liver necrosis associated with such vascular disease as polyarteritis. With these exceptions all cases in which there were classic liver infarcts and all cases in which there were ischemic or hemorrhagic areas of necrosis involving 2 or more contiguous lobules of the liver were included.

Of the 62 cases collected over the 10-year period from 1946-1955, 45, or 72%, occurred in the last 3 years. There were 42 males and 20 females, a ratio of approximately 2:1, and there was a wide range of ages, including 1 newborn infant. Of the total number, 43 occurred in patients in whom some surgical procedure had been performed. In 5 of the 62 patients the hepatic necrosis was associated with direct trauma and in 6 with hepatic vascular occlusion. In the remaining 51 patients no anatomic mechanism for the necrosis was demonstrated. The high correlation between hepatic necrosis and the administration of sympathomimetic amines suggests that this group of drugs may be an important factor in the pathogenesis of the hepatic lesions.

Treating Tuberculosis in a Military Hospital. R. M. Burke and J. A. Wier. U. S. Armed Forces M. J. **8**:963-971 (July) 1957 [Washington D. C.].

The authors studied the records of the tuberculosis section of the Fitzsimons Army Hospital in Denver for the period 1952 to 1955 inclusive and report on the now evolving pattern of management. The patients were young military personnel with recent tuberculosis, civilian dependents (mainly wives of servicemen), and older Veterans Administration patients with predominantly advanced tuberculosis of long duration. The criteria for approved discharge were negative sputum, cavity closure, and roentgenographic stability for from 4 to 6 months. The time required to reach this goal averaged 12 months for patients with minimal disease, 15 months for those with moderately advanced disease, and 15 months or more for those with far-advanced disease. Although the period of hospitalization has been reduced for the military patients by allowing them to complete the last 3 to 6 months of drug therapy while on convalescent leave, the sojourn in the hospital is still longer than that in civilian practice. Only 50% of the military patients treated for active tuberculosis were found to have Mycobacterium tuberculosis in their sputum. Most of the patients with a positive sputum reverted to negativity in 3 months.

All patients with active disease were given chemotherapy for a minimum of 12 months whether the lesions were in the lymph nodes, kidneys, lungs, or bones and joints. Combined therapy with 2 drugs—300 to 450 mg. of isoniazid daily with 12 Gm. of aminosalicylic acid daily, isoniazid with 2 Gm. of streptomycin sulfate every 3 days, or aminosalicylic acid and streptomycin—was employed. As a companion drug aminosalicylic acid appeared to be superior to streptomycin sulfate. Prolonged bed rest is going to play a minor role in the treatment program, since experience with inhospital ambulant treatment has been very encouraging. With this trend a more aggressive inhospital rehabilitation program is possible. In 1954, 50% of the military patients treated to maximum hospital benefits had pulmonary resection. Since then this percentage has been declining, with fewer segmental resections being performed for minimal residuals. This decline appears to be due to an increasing confidence in drugs, particularly isoniazid. Temporary collapse measures have been abandoned. Treatment results of military patients are excellent because discipli-

nary powers result in practically all being treated to the inactive stage of disease. Their relapse rate on follow-up after 3 years of active duty is 3%. The serviceman contracting tuberculosis is now returned to active duty, usually in less than 2 years, where assignments to fit his physical capabilities are provided.

Conservative Treatment of Cholecystitis: Complications and Late Results. S. Lyndrup and K. Kristensen. Ugesk. læger **119**:743-754 (June 13) 1957 (In Danish) [Copenhagen].

Conservative treatment was applied in 272 patients with cholecystitis. Women dominated in all age groups. The total mortality was 17, or 6.2%. Of the 194 patients subjected to conservative treatment, 9 died. Because of compulsory indication, 28 patients were operated on on admission or soon thereafter, in most cases by cholecystolithotomy, with 7 deaths. Perforation of the gallbladder was particularly frequent in male patients; it occurred twice as often in patients aged over 60, and more than half of these died. The material illustrates the surgeon's difficulty in balancing between well-indicated operation and contraindicating general condition. The cases with perforation underline the necessity of early admission, preferably in the course of a few hours, especially for patients over 60. Follow-up of 199 patients for from 5 to 10 years showed 44.2% to be free from symptoms, 24.1% to be relatively well, and 31.7% to be in poor condition or to have been operated on later. Over 40 patients had died at the time of the follow-up. Cancer of the liver, biliary tract, pancreas, or stomach had developed in 7 patients. The authors made the following conclusions: 1. All patients with marked cholecystitis should be hospitalized at once at the start of the attack, this being especially true for older, feeble patients, for whom a few hours' observation at home may endanger life. 2. If conservative treatment is to be instituted, observation must be careful, frequent, and carried out by an experienced clinician. General treatment must be immediate, with adequate fluid and blood administration, possibly with antibiotics and bronchial toilet, and laboratory examinations of liver, pancreas, and kidney function must be carried out often. 3. Operation is advised for all patients with gallstones who have had one attack of severe cholecystitis, if there are no essential contraindications.

The Management of Hepatic Coma in Relation to Protein Withdrawal and Certain Specific Measures. W. H. J. Summerskill, S. J. Wolfe and C. S. Davidson. Am. J. Med. **23**:59-76 (July) 1957 [New York].

The response to treatment was studied in 65 episodes of hepatic coma in 64 patients between the ages of 32 and 76 years, most of whom were alcoholics with severe liver cirrhosis. Hepatic function was the most important factor in prognosis. Of the 63 patients, 34 were treated with a regimen of protein withdrawal from the diet, oral administration of broad-spectrum antibiotics, and enemas, in an attempt to reduce the formation and absorption of toxic nitrogenous substances in the gastrointestinal tract. Twenty-one patients improved during this treatment and 13 recovered. Protein withdrawal and antibiotics reduced arterial blood ammonia concentrations. Thirty of the 64 patients received varying amounts of protein during hepatic coma; 5 patients showed improvement and 2 survived, but the 2 groups were not entirely comparable.

Additional therapy with glutamic acid, aspartic acid, cortisone, hydrocortisone, or lipoic acid was given to 14 of the 34 patients with protein withdrawal therapy and to 26 of the 30 patients who were allowed protein during treatment. No additional significant benefit could be attributed to these specific agents. Like glutamic acid, aspartic acid had a transient effect on blood ammonia values in 2 patients. Lipoic acid had no constant effect on arterial blood ammonia, pyruvate, or alpha-ketoglutarate concentrations. Treatment by protein withdrawal from the diet and with broad-spectrum antibiotics is considered the therapy of choice, but the authors make clear the fact that the problems of pathogenesis and treatment of hepatic coma have not been resolved.

Further Observations on Patients with Malignant Carcinoid. A. Sjoerdsma, H. Weissbach, L. L. Terry and S. Udenfriend. Am. J. Med. **23**:5-15 (July) 1957 [New York].

The authors report on 19 patients with malignant carcinoid. Clinical and laboratory findings in 6 of these patients had been reported by the authors in a previous paper, and the clinical findings in the additional 13 patients confirmed the previous descriptions by the authors and by other workers of a syndrome manifested by vasomotor disturbances, chronic diarrhea, respiratory distress and valvular disease of the right portion of the heart, although some of the patients did not show all these manifestations. A 2-year follow-up of the patients showed that the occurrence of episodic pain over the liver with fever and leukocytosis but negative blood cultures was a frequent complication. These episodes, which usually subsided spontaneously, may have been due to hemorrhagic necrosis of tumor nodules.

Biochemical findings in the previously reported 6 patients consisted of elevated blood levels of 5-hydroxytryptamine (serotonin) and a greatly increased urinary excretion of the serotonin metabolite, 5-hydroxyindolacetic acid (5HIAA). Measurements of serotonin and 5HIAA which were performed on 8 of the 19 patients confirmed previous

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findings of excess serotonin production in this disorder. Also, the findings of low fasting plasma tryptophan and urinary N'-methylnicotinamide in some patients substantiated previous suggestions of a disorder in tryptophan metabolism. A tracer study, which was performed in 1 patient with the serotonin precursor 5-hydroxytryptophan, enabled calculation of the tumor pool of serotonin (2,800 mg.), its turnover rate (half life of 5½ days), and the tumor mass (between 1 and 3 kg.). Increases in the urinary excretion of 5HIAA in a patient during severe flushing episodes suggested that the flushes were mediated by increased serotonin release, though no concomitant rise in the blood serotonin level could be measured. Cardiac catheterization studies revealed no measurable differences in the serotonin content of mixed venous and arterial blood which, if present, might account for predominant involvement of the right side of the heart. It is suggested that if a pulmonary arteriovenous serotonin difference does exist, it is in that portion which is free in the plasma. The absence of serotonin in cerebrospinal fluid and the essentially negative results of psychological evaluation seemed to indicate that serotonin does not penetrate readily into the central nervous system.

With the possible exception of chlorpromazine, drug therapy has proved ineffective. The administration of chlorpromazine appeared to decrease the frequency and severity of flushing reaction, to allay anxiety, and to control the nausea which afflicted some of the patients. Although reports in the literature suggest that chlorpromazine antagonizes certain effects of serotonin, it is possible that the efficacy of chlorpromazine in patients with carcinoid is unrelated to interaction with serotonin. An agent which effectively blocks the physiological effects of serotonin would be a useful addition to the management of patients with malignant carcinoid.

Determination of 5-Hydroxytryptamine, 5-Hydroxyindole Acetic Acid and Histamine in 33 Cases of Carcinoid Tumor (Argentaffinoma). B. Pernow and J. Waldenström. Am. J. Med. **23**:16-25 (July) 1957 [New York].

Determinations of 5-hydroxytryptamine (serotonin, 5HT) in the blood serum and urine and of 5-hydroxyindole acetic acid (5HIAA) in urine were made in 33 patients with abdominal carcinoid tumor (argentaffinoma). The patients were divided in 2 groups. The first group consisted of 22 patients with metastatic abdominal carcinoid tumor in whom the determinations of serotonin and its metabolite were made before operation or in whom the tumor was not completely resected. The second group consisted of 11 patients in whom probably complete resection of the tumor had been performed. The 5HT analyses showed increased values in blood and/or urine in 17 patients of the first group, with figures ranging from 0.15 to 5.2 mcg. per cubic centimeter of blood serum and 0.1 to 4.2 mcg. per cubic centimeter of urine. Abnormally high 5HIAA values ranging from 14 to 452 mg. per 24 hours were obtained in 19 patients. In the second group of patients the 5HT and 5HIAA figures were normal or slightly increased.

The urinary excretion of histamine was also studied in 8 of the 22 patients in group 1 and in an additional patient who had a malignant tumor of unknown primary site with metastases to the lungs and skeleton; biopsy of a skeletal metastasis revealed a carcinoma of unknown type, possibly a carcinoid. Increased excretion of histamine was observed in 7 of these 9 patients, with figures ranging from 27 (borderline value) to 6,800 mcg. per 24 hours. The fact that both histamine and 5HT were found in increased amounts in the urine of these patients suggests some relationship between these substances in the body. It might be assumed that the tumor cells produce both 5HT and histamine. Another explanation might be that increased formation of 5HT in the tumor cells leads to secondary release of histamine.

One patient in the first group was of unusual interest because of high values for 5HIAA in her urine, chronic flushing of the face, signs of pulmonary heart disease, and "pellagra." The microscopic examination of tissue removed at operation revealed a nonmalignant ovarian teratoma with argentaffine cells in large numbers. After operation all symptoms (except the cardiac) disappeared, and the excretion of 5HIAA has remained normal.

Davidson's Megaloblastic Anemia. M. Georgescu and L. A. Long. Presse méd. **65**:1056-1057 (June 5) 1957 (In French) [Paris].

The authors treated successfully with folic acid 2 patients with idiopathic refractory megaloblastic anemia and with hydrochloric acid in the gastric content. In 1948 Davidson reported on 25 cases of idiopathic megaloblastic anemia, refractory to highly purified and concentrated liver extracts administered intramuscularly. These extracts were, however, very active in Biermer's pernicious anemia. Davidson suspected, therefore, that there is a hemopoietic factor in the liver that is destroyed during the purification of the liver extract. He demonstrated that this factor was folic acid, which was very active both in cases of Biermer's anemia and in idiopathic megaloblastic anemia. Folic acid was ineffective in some cases, whereas the extract of the proteolysis of the liver proved highly effective. Davidson thought that there must be other

active factors not yet isolated. Later it was proved that folic acid must be reduced to folinic acid to be effective. Vitamin B^{12} acts only as a factor liberating folic acid. In Biermer's pernicious anemia there is a lack of vitamin B^{12}, whereas in Davidson's anemia there is a lack of folic acid. It is not understood why certain types of idiopathic megaloblastic anemias respond to purified liver extract and to vitamin B^{12}, whereas others resist this therapy but respond to folic acid or to the extract of the proteolysis of the liver. Vilter conjectures that vitamin B^{12} and folic acid intervene at different stages of the chain reaction leading to the formation of normoblastic nucleic acids. Folic acid, transformed in the organism into folinic acid, acts at the initial stages catalyzing a synthesis of pyramidines, whereas vitamin B^{12} enters at a later stage of transformation of pyramidines into nucleosides. According to Vilter, lack of vitamin B^{12}, which enters only at a late stage in the chain reaction, causes only one type of difficulty, which is Biermer's anemia. The absence of folic acid, which acts at the initial stages, causes various types of refractory megaloblastic anemias, such as megaloblastic anemia of obesity, infant's anemia, anemia of liver disease, anemia of tropical and nontropical sprue, and idiopathic refractory megaloblastic anemia. The exact relationship between vitamin B^{12} and folic acid is still not clear. It is known, however, that deficiency of vitamin B^{12} entails in the long run a secondary deficiency of folic acid.

Rheumatoid Arthritis of the Cricoarytenoid Joints. W. S. C. Copeman. Brit. M. J. 1:1398-1399 (June 15) 1957 [London].

Rheumatoid arthritis has been described affecting almost every diarthroidal joint in the body and should be extended to include the cricoarytenoid joints. These joints are small, extremely mobile, and involved in phonation and normal full respiration. The muscles controlling the movements of the cricoarytenoid joints are innervated by the recurrent laryngeal branch of the vagus. Unilateral paralysis of this nerve is common and causes hoarseness, but not loss of voice. Bilateral paralysis of the nerve results in loss of voice and stridor on deep respiration. Three cases are described which demonstrate the varying stages in this syndrome, e. g., acute and subacute recurrent laryngeal episodes and complete ankylosis of both cricoarytenoid joints in the final stage of rheumatoid disease. The differential diagnosis in these cases lies only between rheumatoid arthritis involving the cricoarytenoid joints and paralysis of the recurrent laryngeal nerves. The involvement of the cricoarytenoid joints may occur as an integral part of the polyarthritic process.

SURGERY

Spontaneous Subcortical Haemorrhage in Young Adults: A Report of 7 Surgically Treated Cases. R. A. Daws. Brit. J. Surg. 44: 583-588 (May) 1957 [Bristol, England].

The author reports observations on 7 patients with intracerebral hemorrhage who ranged in age from 19 to 34 years and who were treated surgically. With one exception, angiography failed to show vascular malformation. Hypertension was absent, and there were no clinical signs of arterial disease. Syphilis was excluded in all but one of the patients by serologic tests. There was no history of head trauma. Angiography raised the question of a congenital angiomatous malformation in 1 patient, and in this patient this seemed to be the most likely explanation of the cerebral hemorrhage, although there was no history to suggest such a lesion. Hemorrhage, however, is a recognized complication of these congenital malformations and may well be the presenting symptom. The fact that the vascular abnormality could not be demonstrated on repeat angiography after the recovery of the patients may be of some significance in the question of etiology in these cases in general. It is possible that after the rupture of the angioma, with the formation of an intracerebral clot, partial destruction of the lesion occurred and this was followed by thrombosis in the remainder. Operative experience with these malformations has shown that if the arteriovenous shunt is removed then the secondarily dilated vessels will revert to normal. Disruption of the shunt as the result of hemorrhage would presumably have the same effect.

The most important feature of the clinical picture was the sudden onset of the illness and the gradual progression of the symptoms. The patients, apparently in perfect health, were suddenly struck down, but the dramatic picture usually associated with adult apoplexy did not occur, and there was no loss of consciousness unless epilepsy supervened. Headache was present in all but one patient. Vomiting occurred as an early symptom in 4 of the 7 patients and during the course of the illness in 2. Focal disturbance of cerebral function was an early and often presenting feature. In all but one patient hemiparesis, of varying severity, was a prominent sign and was frequently associated with a disturbance of sensation. Dysphasia was also commonly present. Raised intracranial pressure occurred in all but one patient as shown by the presence of papilledema or raised pressure on lumbar puncture. In 4 of the 5 patients who had a lumbar puncture performed there was evidence of some bleeding into the cerebrospinal fluid. The choice of operation rests between (1) simple aspiration of the fluid part of the hematoma through a bur-

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hole and (2) craniotomy and the complete evacuation of the clot under direct vision. The latter is the operation of choice. Five of the 7 patients recovered completely, but 2 have a moderately severe residual hemiparesis with sensory loss. This shows that with surgical treatment the prognosis is relatively favorable.

Effect of Division of the Hypophysial Stalk in the Hypertensive Patient. C. Keedy. Am. Surgeon **23**:439-447 (May) 1957 [Baltimore].

The author presents the histories of 5 patients in whom the hypophysial stalk was divided to observe the effect on hypertension. The group included 2 men and 3 women, ranging in age from 33 to 55. The patients have been followed for from 1 to 5½ years. One showed no significant change but was completely relieved of her headaches. One patient with secondary hypertension due to renal disease showed marked lowering of her blood pressure but a slowly progressive downhill course terminating in death from renal failure without elevation of the blood pressure. This suggests that the neurohypophysis is involved in the mechanism that produces renal hypertension and tends to confirm the work of Sattler and Ingram in dogs. Two patients showed disturbance of gonadotropic hormone, 1 by amenorrhea and 1 by mild gynescomastia. Temporary diabetes insipidus occurred in 1 patient. Two patients with hypertensive encephalopathy with convulsive seizures preoperatively have had no further seizures. Two patients who had evidence of cardiac failure preoperatively have had no evidence of it postoperatively. One patient had severe optic atrophy and 1 has mild optic atrophy. The best fall in blood pressure after operation was observed in those patients who showed a lowering of the blood pressure after therapy with etamon chloride or sodium amytal. No definite conclusion can be drawn from these meager observations, yet the results suggest that section of the pituitary stalk in a hypertensive patient (1) will produce significant lowering of the blood pressure in most patients, (2) will not produce permanent diabetes insipidus, and (3) may produce signs of gonadotropic hormonal deficiency.

The Prognosis of Atrial Septal Defect. M. Campbell and C. Neill. Brit. M. J. **1**:1375-1383 (June 15) 1957 [London].

Atrial septal defect as a recognized clinical entity was first described in this country by Bedford. Since that time, the diagnosis had been made with confidence and increasing frequency. Of the many young children seen with the classic picture of atrial septal defect, nearly all were thin and slightly built, with long, narrow chests and limbs (gracile habitus) and pigeon breasts. They exhibited remarkably few signs and/or symptoms and possessed large hearts. The most characteristic physical sign is the gross discrepancy between the small pulse and the widespread overactive precordial pulsation. This excessive pulsation has 3 components: (1) an apex beat that is tapping in character and is displaced outward, (2) a right ventricular thrust or lift that is usually visible and almost always palpable in the third left intercostal space, and (3) a large pulmonary artery that may give rise to visible systolic pulsations in the second space. Wide splitting of the second heart sound has been valuable as a diagnostic aid. Radiological studies show the triad of a large right side of the heart, large pulmonary artery, and a hilar dance with expansile pulsation spreading to smaller branches. Negative findings equally important in diagnosis are absence of enlargement of the aorta, of the left ventricle, and of the left atrium. The electrocardiogram is characterized by increased QRS length, rSR′ pattern, no real primary and secondary R waves, and some notching of the R waves. Differential diagnosis of this defect must preclude ostium primum, anomalous pulmonary venous drainage, ventricular septal defect, and simple pulmonary stenosis. The most common cause of heart failure and death was found to be failure of the right side of the heart, followed closely by pulmonary hypertension with central cyanosis, severe symptoms with some rise of pulmonary pressure, failure of the left side of the heart, and pulmonary embolism, in that order. Prognosis is excellent in children, diminishing somewhat in the third decade and becoming progressively poor in successive decades. The onset of auricular fibrillation in these cases is serious, with death following almost inevitably within the year. Mitral stenosis in patients with this defect obscured the wide-splitting second heart sound.

Indications and Results of Mitral Commissurotomy. G. Invernizzi. Sett. med. **45**:135-139 (March) 1957 (In Italian) [Florence, Italy].

The authors report on 26 patients, 17 to 46 years old, subjected to mitral commissurotomy. The decision to operate was reached in each patient after consideration of the extent and form of the pulmonary tension, the condition of the myocardium, and the extent and form of the valvular obstruction. Five patients suffered a progressive cardiac insufficiency which compelled them to stay in bed; 15 presented sporadic episodes of decompensation and dyspnea, in some patients only on exertion; and 6 patients presented subjective symptoms only. There were no operative deaths; 2 patients died within the first month after the operation. Commissurotomy was beneficial to all patients except one. Dyspnea and pulmonary edema disappeared, and the patients responded to cardiokinetic drugs. A

slight change in auscultatory findings occurred in 4 patients only. Pleuropericarditis in the left side was observed in more than half of the patients. Observations made 6 months to 5 years after the operation revealed persistence of the improvements. Of special interest were 6 patients with mild preoperative functional disturbance who were operated on in view of eventual stress they were facing (delivery, pregnancy, major operation, or need to employ exertion in their work). The success obtained in these patients opens the way to the consideration of mitral commissurotomy as a prophylactic measure.

Perforation of Stress Ulcers of the Esophagus Following Thermal Burns. J. R. Derrick, A. H. Wilkinson and J. M. Howard. A. M. A. Arch. Surg. **75**:17-20 (July) 1957 [Chicago].

Evidence is cited in this report of 2 cases that perforation and rupture of the esophagus previously considered as separate entities, can be present in combination, as ulceration of the mucosa weakens esophagus to such an extent as to predispose it to rupture from even so minor a stress as vomiting. Autopsy findings in 2 patients who had sustained 90 to 95% third-degree burns indicated an ulcerated mucosa and rupture at the site of ulceration. The antemortem diagnosis of esophageal rupture was not made, and it is not made in 75-85% of those persons with nontraumatic perforation. The predilection to rupture and/or perforation of the esophagus is further augmented by incoordinate vomiting, ulceration, esophagitis and general lack of support in the lower portions of the esophagus. The dominant factor in alimentary canal perforation is not the degree of pressure per se but rather the rapidity with which the intraluminal pressure is increased. Severe thermal trauma, possibly by initiating the alarm reaction, has resulted in acute esophageal ulcerations within hours, both clinically and experimentally. Rupture not associated with intrinsic disease or ulceration is postulated as being due to incoordination of the vomiting mechanism, spontaneous perforation having been reported in association with central nervous system disease, pyloric obstruction, or chronic vomiting.

The Abuse of Intestinal Intubation. J. J. Farrel and G. B. Reams. Am. Surgeon **23**:401-408 (May) 1957 [Baltimore].

Nasogastric suction and intestinal intubation as adjuvants in the treatment of intestinal obstruction have, rightfully, been credited with a significant contribution in the lowering of mortality rates in these conditions. However, failure to be cognizant of the inherent dangers and difficulties of intubation has resulted in 2 major ills: (1) the relegation of the intubation and subsequent management thereof to the least experienced of house officers and through them to the nursing staff; (2) the unwise selection of a tube predicated on its reputed ability to be more easily passed through the pylorus and the increased intraluminal size of the tube. Analysis of the complications occurring with intubation demonstrates that most of these are associated with prolonged use of intubation as a definitive measure rather than its utilization as a preoperative and postoperative adjuvant. While necrosis, knotting, and perforation can occur rapidly, these and the subsequent inability to withdraw the tube are usually associated with the utilization of the tube for a period of several days. Prolonged usage of these tubes is also followed by an increased rate of upper respiratory complications associated with excessive nasopharyngeal secretions from irritation of the tube, otitis media, nasopharyngeal abscesses, and stenosis of the larynx and esophagus. In addition, it must be remembered that a tube in the small intestine does not necessarily remove accumulated fluids in the stomach itself, and vomiting with aspiration can and does occur.

The authors present the histories of 7 patients to illustrate the abuse of intestinal intubation. One patient died shortly after an operation for multiple perforations of the small intestine, resulting from traction during attempts at removal of the tube. In another patient a Harris tube was left in place an extended length of time and became knotted. Observations on other patients show that a balloon should be used in which excess air can be removed with the tube in place; that the addition of mercury to a deflatable balloon tube defeats its purpose, in that the mercury rarely if ever can be withdrawn successfully; that some tubes will not pass through the entire intestine and must be removed surgically; that persistent efforts to remove a tube may lead to necrosis of the intestinal wall; and that, while free mercury in the intestinal tract may cause no difficulty, there have been reports of fistula formation and abscesses with lodging of the mercury in diverticula.

Bronchial Adenoma. K. Fraser. Brit. J. Surg. **44**:570-581 (May) 1957 [Bristol, England].

The wider use of bronchoscopy in the examination of persons with chest disease has demonstrated that bronchial adenoma is not as rare as it was formerly believed to be. The author reports findings on 12 patients observed in the course of 13 years in a thoracic surgery unit of a Glasgow hospital. Bronchial adenoma is tumor of slow growth, almost invariably arising in relation to a stem bronchus of a lobe or lung; consequently it was seen on bronchoscopic examination in every one of the 11 patients bronchoscoped. The gross characteristics of these tumors are so typical that the bronchoscopist can often suggest the diagnosis. There is partial or complete occlusion of a stem

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bronchus to a lung or lobe by a lobulated pink, red, or purplish mass which is firm to the touch and bleeds readily. The surface of the tumor is smooth, because as a rule the bronchial mucosa has not ulcerated, though ulceration may develop and squamous metaplasia may occur. An important feature is that some of these tumors resemble an iceberg floating in water, in that the visible portion is much smaller than the portion lying within the lung substance. The usual tumor might be likened to a dumb-bell. It has a small intrabronchial portion joined by a narrow neck of tumor which passes through the cartilaginous rings to the main mass lying in adjacent lung tissue, which is compressed around it. If the adenoma partly or completely blocks the bronchus into which it projects, the lung distal to the obstruction will show pathological changes such as segmental or lobar atelectasis.

Unlike carcinoma of the lung, adenoma occurs much more frequently in women than in men, the incidence in this series being 10:2. The age distribution in adenoma is usually below 40 years and often between 20 and 30. Cough is the most frequent symptom; it may be dry or be accompanied by frothy mucoid sputum. Recurring hemoptysis is also relatively frequent. Other symptoms associated with adenoma arise as a result of obstruction to the bronchus in which the tumor lies. All 12 patients were treated surgically. One tumor was successfully removed through the bronchoscope, but the patient subsequently required lobectomy to remove diseased lung tissue, while 1 tumor was removed by bronchotomy. Three others were adequately dealt with by lobectomy, and 2 required removal of both middle and lower lobes. The remaining 5 required pneumonectomy, but in 2 patients an erroneous diagnosis of oat-cell carcinoma had been made, and lobectomy might have been sufficient. The author believes that in former years patients with bronchial adenoma either died at home under the mistaken diagnosis of unresolved pneumonia or carcinoma, or they died in sanatoriums erroneously given the diagnosis of tuberculosis.

Malignant Anorectal Melanoma. G. Cristiani, S. Sokol and O. Eguía. Prensa méd. argent. **44**:494-498 (Feb. 15) 1957 (In Spanish) [Buenos Aires].

Anorectal melanoma is a rare and highly malignant tumor. It develops from the pavement epithelium of the anal canal and involves the rectum. The early symptoms are enlargement of the inguinal lymph nodes, anorectal pain, rectal hemorrhages, and rectal tenesmus. The diagnosis is made by biopsy. The authors observed 2 cases in women 50 and 70 years old, who were cared for in an oncologic clinic. The patients complained of anorectal symptoms of 6 months' and one year's duration, respectively, of great loss of weight, and of a rectal tumor. The inguinal lymph nodes were enlarged. Diagnosis of malignant melanoma was made by biopsy. In the younger patient the operation consisted of abdominoperineal resection of the anal, rectal, and sigmoid segments followed, in 3 weeks, by bilateral dissection of the inguinal lymph nodes. Histological examination of the tumor confirmed the diagnosis. The lymph nodes showed metastases of a malignant melanoma. The patient survived 21 months after the operation, 18 months in fairly good general condition, the last 3 months manifesting deterioration leading to death. In the older patient a roentgen examination revealed metastases in the lung. She was subjected to palliative procedure of a sigmoid colostomy and perineal amputation. Histological study of the removed specimen confirmed the clinical diagnosis. The lymph nodes had metastases of malignant melanoma. The patient survived 5 months. At autopsy, metastases were noted in the lungs, heart, liver, gallbladder, stomach, small intestine, kidneys, adrenal glands, lymph nodes of the lesser and greater curvatures of the stomach, and the intrathoracic lymph nodes.

The Management of Penetrating Wounds of the Inferior Vena Cava. T. E. Starzl, R. K. Broadaway, R. C. Dever and G. B. Reams. Am. Surgeon **23**:455-461 (May) 1957 [Baltimore].

Histories are presented of 3 patients who sustained gunshot wounds of the inferior cava and who were successfully treated with suture repair. These represent the 8th, 9th, and 10th cases of missile injury to the inferior cava, with survival, in the literature. Recovery in 1 patient was complicated with external iliac thrombosis. One of the patients had an associated aortic laceration, also sutured. All the patients had additional multiple serious visceral injuries. One of the caval injuries was above the level of the renal veins; this is the second such case in the literature. In these 3 patients, as well as almost all others in the literature, massive bleeding had ceased by the time celiotomy was done. It is quite possible that, with this spontaneous tamponade, no further venous hemorrhage would occur if the retroperitoneal space were not explored. It is, however, not possible for the surgeon to be certain of this, and it is frequently necessary (as in the present series) to carry out such exploration for other retroperitoneal injuries which, if left untreated, would be fatal. Therefore, when the trajectory of a missile projects to or near the great vessels, the authors believe that a program designed to give exposure of the potentially injured vessel should be instituted. There is no need for haste, since recurrence of hemorrhage need not be anticipated until the retroperitoneal dissection is begun. Lighting can be adjusted, vascular instruments obtained, additional assistants summoned, and additional blood crossmatched.

During this period of preparation, manipulation of the hematoma should be avoided because, by probing or manipulating, the surgeon may precipitate a massive hemorrhage at a time when he is ill-prepared to deal with it. For caval injuries at or below the transverse mesocolon, the authors approach the retroperitoneal space by reflection of the small intestine and its mesentery to the right, or by reflection of the ascending colon to the left. The ultimate in exposure is gained by a combination of these maneuvers, reflecting the small intestine, ascending colon, and related mesenteries in a cephalad direction. For injuries above the transverse mesocolon, the hepatic and transverse colon as well as the transverse mesocolon are swept inferiorly. The retropancreatic area can then be entered with wide exposure with the Kocher maneuver. The authors are of the opinion that postoperative anticoagulation therapy is not routinely necessary but should be considered in multiple or unusually severe caval injuries.

Sepsis in Surgical Wounds with Particular Reference to Staphylococcus Aureus. B. K. R. Clarke. Brit. J. Surg. 44:592-596 (May) 1957 [Bristol, England].

Wound infection was studied in 2 general surgical wards over a period of 10 months. The part of the investigation concerned only dry wounds and drained wounds. Suprapubic and colostomy wounds were not considered. Dry wounds can be defined as undrained wounds which normally heal by first intention. They rarely became infected. Drained wounds often became infected. Out of the 382 dry operation wounds investigated, 52 (13.6%) broke down; that is, they healed by secondary intention. These included wounds from operations such as appendectomy and partial gastrectomy involving the opening of unsterile viscera. In 27 (7.1%) the break-down was minimal, but in 25 (6.5%) it was moderate to severe. The most common cause of severe break-down was the bursting of deep abdominal abscesses yielding coliform bacilli. The second most common cause was sepsis due to Micrococcus (Staphylococcus) pyogenes var. aureus. These infections were almost always acquired in the operating room, and half of them were penicillin-sensitive. Minor inflammation in healing dry wounds was commoner 6 to 8 days after operation than at other times; it was commoner in wounds closed with stitches only than in those closed with clips; and it was commoner in wounds heavily infected with M. albus than in those lightly infected or not infected. Strains of penicillin-resistant M. aureus caused as severe lesions as did strains of penicillin-sensitive M. aureus. M. aureus is coagulase-positive, and M. albus is coagulase-negative.

The average length of stay in hospital of patients whose wounds were infected with M. aureus was found to be 5 days longer than the average length of stay of patients whose wounds were not so infected. However, many patients stayed in hospital for more than the usual length of time for reasons not connected with micrococcic infection. These patients, then, owing to their long stay in hospital, acquired M. aureus in their wounds. Again, patients who had had operations which necessitated their staying in hospital for a long time had also the type of wound which often acquired M. aureus. Also, in the ward where fewer wounds became infected with M. aureus it was the custom to send the patients home in the shortest possible time after operation, unlike the custom in the other ward.

NEUROLOGY & PSYCHIATRY

Epidemic of Aseptic Viral Meningitis Associated with Eruption: A New Clinical Entity. J. Valcke and E. Nihoul. Arch. franç. pédiat. 14:553-562 (No. 6) 1957 (In French) [Paris].

The authors report on an epidemic of nonbacterial meningitis which occurred in Belgium in the summer of 1956 and which attacked about 3,000 persons. Similar outbreaks were reported from the Netherlands, Germany, Switzerland, Great Britain, and Denmark. The authors studied the clinical course of the disease in 95 children and 19 adults in 58 families. One member was ill in 32 families, and the number of sick members varied from 2 to 9 in the other 26 families. These 114 patients were divided in 4 groups. Forty infants and 11 adults had a pronounced meningeal syndrome associated with an eruption of a character midway between scarlet fever and measles. A mild meningeal syndrome was present in 37 children and 8 adults. Twelve children had a general, infectious, influenza-like syndrome with fever and eruption, and 6 children had a mild syndrome of influenza with vague symptoms of infection and without eruption. Lumbar puncture was performed in 39 children, 35 of whom belonged to the 2 first groups, 3 to the third group, and 1 to the 4th group. The cerebrospinal fluid of patients in the first 2 groups contained a fairly large number of cells, varying from 200 to 2,000 per cubic millimeter. The course of the disease, which was always benign, varied considerably. It did not depend on the therapeutic methods used. Antibiotics were ineffective, and treatment was mostly symptomatic, i. e., antipyretic and analgesic. The usual duration of the disease was 1 week. After a brief drop in temperature, there was a second rise. Many patients seemed to have a recurrence of the disease after an apparent recovery.

Poliomyelitis viruses and Coxsackie viruses were excluded as causative agents. The laboratory diagnosis was established by isolation of the virus from feces and from the cerebrospinal fluid, by crossed serologic (neutralization) tests, and by identification

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of all the isolated viral strains as enteric cytopathogenic human orphan (ECHO) viruses, type 9. For the first time this virus has been demonstrated as a causative agent in an epidemic. Encephalomyelitic symptoms such as headache, vomiting, pain in the neck, and a large number of cells in the cerebrospinal fluid were observed only in patients in whom this virus was demonstrated.

Influence of Age and Sex on Susceptibility and Clinical Manifestations in Poliomyelitis. L. Weinstein. New England J. Med. **257**:47-52 (July 11) 1957 [Boston].

The author studied the importance of age and sex in determining the nature of poliomyelitis in 618 patients with the paralytic form of the disease observed by him from 1950 through 1955. One hundred patients were 5 years old or less; 161 were between 6 and 15 years of age; 213 between 16 and 30; 117 between 31 and 39; and 27 between 40 and 65 years of age. Poliomyelitis was more severe in adults than in children, as indicated by the greater frequency of urinary dysfunction, quadriplegia, respiratory paralysis, and death in persons over the age of 16 years. When monoplegia occurred, the left side was involved more often than the right, especially in adults. There appeared to be a sex predisposition to susceptibility to poliomyelitis; among children, there was a preponderance of males, but in adults, there was a small excess of females. Among children up to 16 years old the male to female sex ratio was 63.2 to 36.8; in 330 adults between 16 and 39 years of age women outnumbered men (53.4 to 46.6). A striking reversal of this trend was noted in persons between 40 and 65; of the 27 patients in this group 20 (74%) were men and 7 (26%) were women.

In adult patients, quadriplegia, respiratory paralysis, and death occurred more frequently in men than in women, despite the greater number of women in this age group. In men over 40 poliomyelitis is most likely to be severe and fatal; next in order of risk is the male 16 to 39 years of age. Because of the high risk of severe, permanent crippling and death, it is just as important to immunize all adults against poliomyelitis as it is to protect all children, despite the lower incidence of the disease in the older age group.

Nonneurological Lesions of Poliomyelitis in the Acute Phase. G. C. Angela and F. Di Nola. Minerva med. **48**:2149-2157 (June 20) 1957 (In Italian) [Turin, Italy].

The authors report on a study of the anatomic and pathological nonneurological lesions present in a group of 198 patients with poliomyelitis in the acute phase. Fourteen patients died of bulbar poliomyelitis and 1 of intercurrent bronchopneumonia. Postmortem examination of the 15 patients revealed interstitial lesions and lesions of the bronchioles in 4 patients, bronchopneumonic lesions in 1, mechanical obstructive phenomena in 7, and pulmonary edema in 1. Pulmonary lesions were not present in the other 2 patients. Specific myocarditis due to poliovirus was not found. Examination of the heart showed signs that are frequently found in patients dying of other infectious diseases or of acute asphyxia. One patient presented mild hemorrhagic lesions in the gastric mucosa and in the terminal part of the ileum. Some patients presented skin lesions which were caused mainly by muscle dysfunction. Phenomena of hyperkeratosis and at times of acanthosis with contraction and rupture of the elastic fibers were noted in some patients; these lesions were more marked in the elderly patients. Significant osteoarticular lesions were not observed. The patients were dismissed as soon as they had recovered from the acute phase of the disease, whereas osteoarticular lesions occur at a later stage. Early atrophic phenomena combined with inflammatory infiltrates (lymphocytes and rarely plasmacytes) were observed in the muscular fasciculi at autopsy and at biopsy.

Histopathological Study of Acute Anterior Poliomyelitis: Lesions of the Peripheral and Central Sensory Systems. S. Nicolau, T. Hornetz, R. Dinu and others. Minerva med. **48**:2168-2176 (June 20) 1957 (In Italian) [Turin, Italy]

The topography and the extension of the lesions in the sensory neurons of the spinal cord, in the peripheral segments (ganglions and nerves); the alterations of the general sensibility in the various regions of the encephalon, from the bulb to the thalamus and to the cerebral cortex; and the centers of unconscious proprioceptive sensibility in the cerebellum were studied in 52 patients with poliomyelitis and in 4 monkeys that had been infected with poliovirus. All patients presented lesions of the posterior horns; the lesions were more marked at the base of the horns (the region most close to the anterior horns) in half of the patients. Three patients had true lesions only in the posterior horns, while perivasculitis was observed in the anterior horn. Five of 14 patients with lesions in the sensory area presented massive softening of the posterior horns. Involvement of Clarke's column occurred in 5 patients. A study of the medulla by longitudinal serial sections in 3 patients revealed uninterrupted lesions.

Lesions of the spinal ganglions were always present. Cajal cells were found to participate very actively and from the very beginning in the neuronophagic process. Diffused infiltration with lymphocytes and monocytes and connective tissue hyperplasia were observed. Lesions of the roots were pronounced whenever the grey substance was

markedly affected. Fairly intensive perivascular infiltrations were observed in some patients. One patient with extensive lesions of the roots presented a discontinuous and segmentary degeneration of the peripheral nerves.

The study of the sensory encephalic connections in 5 patients revealed lesions of the bulb, of the protuberance, and of the peduncle as well as of the cerebellum and of the thalamus in 3 patients. The other 2 patients presented lesions that went beyond the bulb but did not have lesions of the neurons in the parietal region of the cerebral cortex. Observations in 20 patients showed that in 7 patients the spinal ganglionic lesions were as intensive as the lesions of the corresponding posterior horn.

Encephalitis After Varicella. P. Bergsjø. Tidsskr. norske lægefor. 77:518-519 (June 15) 1957 (In Norwegian) [Oslo].

Encephalitis after varicella is believed to occur less often than encephalitis after measles. Adult varicella patients often have headache and pain in the back, which may indicate a slight degree of encephalitis. The recognized cases occur most often in children aged from 4 to 8. The prognosis is more unfavorable in adults. Varicella encephalitis usually sets in from the 3rd to the 8th posteruptive day. Report is given of a case of encephalomyelitis after varicella in a boy aged 7, with onset on the 7th posteruptive day. The boy was in coma for 3 weeks. Two days after one attack of generalized convulsions, treated with barbiturates in large doses, hyperpyrexia and circulatory collapse occurred. The blood pressure returned to normal after administration of norepinephrine in glucose, and the temperature fell after hibernation with cold sheets and ice bags, treatment believed to have been life-saving at this critical stage. Continuous oxygen, penicillin, and streptomycin were given prophylactically, with fluids intravenously. Six weeks after his awakening from the coma the boy shows no signs of psychic changes and there is improvement in the muscular weakness.

GYNECOLOGY & OBSTETRICS

Malignant Vulvar Paget's Disease. J. D. Woodruff and E. H. Richardson Jr. Obst. & Gynec. 10:10-16 (July) 1957 [New York].

The authors report the occurrence of Paget's disease of the vulva with cellular alterations suggesting malignant change in the Paget cells in 2 women aged 64 and 62 years respectively. The illness of the first patient began about 3 years before her admission to hospital with the appearance of a small pimple on the left vulva; there had been marked pruritus associated with the lesion, and the patient had received cortisone and corticotropin (ACTH) both locally and parenterally, with temporary improvement. A relapse was treated unsuccessfully by x-ray therapy. On admission, pelvic examination showed marked redness and edema of the left labium. There were numerous small white islands scattered throughout the brilliant red lesion. The edges were sharply demarcated. The clitoris, right vulva, and left perineum and buttock were involved. A biopsy of the lesion revealed intraepithelial carcinoma, and a total vulvectomy was performed. Microscopic examination of the specimen showed that most of the epithelium was thickened and distorted by masses of large clear cells with pale fine granular cytoplasm; most of the nuclei were pale and only a few were hyperchromatic. Degeneration with vascuolization was prominent. These same cells were seen diffusely throughout the ducts of the sweat glands and also in the root sheaths of the hair follicle. The acini of the apocrine and merocrine glands were infiltrated with individual cells of the type described in the surface epithelium. The microscopic picture thus was that of rather striking individual cell anaplasia with definite involvement of the underlying epithelial structures. In several areas there were masses of these cells obliterating the acini, and forming a definite adenomatous tumor, not unlike the comedocarcinoma of the breast. Five and one-half months later an area in the perineum and buttock to the left of, and below the level of the scar at the fourchette, was excised, and characteristic cells were found in surface and ductile epithelium with marked nuclear variation in size and staining qualities. Six months later a small area to the left of the urethral meatus and another to the right of the fourchette were excised, and the epithelium was again thickened and characteristic cells were quite prominent. The patient remained well, with no local recurrence to date.

The second patient was admitted to hospital because of enlarged left inguinal lymph nodes and a history of eczema of the vulva of 8 years' duration. She presented the typical picture of a malignant tumor of the vulva with massive involvement of inguinal lymph nodes. A radical vulvectomy was performed. The microscopic picture again was that of a rather marked individual cell anaplasia. In many sections, the absence of any underlying tumor was striking, and the only tissue breakdown was in the tumor growth itself. The normal epithelium was distorted, but there was little if any evidence of local destruction such as that seen in most of the malignant tumors. Twelve months later a recurrent tumor in the perineal region was excised with removal of left superficial inguinal and femoral lymph nodes, which showed metastatic tumor. The patient received deep x-ray therapy which was discontinued because of lack of response. Although the patient gradually deteriorated physically as a result of the

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malignancy, the progress was slow when compared with the usual course of malignant disease. Death occurred 15 months after the vulvectomy, and autopsy revealed squamous-cell carcinoma of the vulva with extension to uterus and tubes and metastases to inguinal and retroperitoneal lymph nodes, skin, peripancreatic tissue, and obstruction of the duodenum secondary to metastatic lesions.

Paget's disease of the vulva is a distinct entity. The clinical picture and the course are usually that of an intraepithelial carcinoma which may involve any of the structures of ectodermal origin, most commonly the apocrine glands, with which there seems to be a definite anatomic association. When malignancy does occur, metastatic spread seems to be slow and involves adjacent areas and regional lymph nodes first. The metastases show clusters of cells which often contain scattered clear cells similar to that seen in the original tumor. Treatment should consist of wide local excision and frequent follow-up biopsies in the local area. Unless macroscopic or microscopic evidence of malignancy is present, no further therapy would seem necessary. In the presence of such evidence, lymphadenectomy would definitely be indicated, since not only does the tumor seem to be slow growing, but also x-ray therapy has been of no value.

Management of Toxemia of Pregnancy with Reserpine: I. Maternal Effects. S. F. Rogers, J. E. Lindley, J. H. Moyer and M. Desmond. Obst. & Gynec. **10**:17-27 (July) 1957 [New York].

Of 303 pregnant women with toxemia given reserpine alone and in combination with hydralazine hydorchloride, 95 had severe preeclampsia, 25 had primary hypertensive disease with severe preeclampsia, 169 had mild preeclampsia, and 14 had eclampsia. The patients with mild preeclampsia were given 5 mg. of reserpine intramuscularly or intravenously. This dose was repeated in 1 or 2 hours if the patient was still hypertensive. Thereafter, 5 mg. of the drug was given every 4 to 6 hours intramuscularly, as needed, to maintain a blood pressure of 140/90 mm. Hg or higher. Five to 10 mg. of hydralazine intravenously, either as a single injection or a slow intravenous infusion with 25 mg. of the drug to 100 cc. of 10% dextrose in water, was given only when a normotensive response was not obtained with reserpine alone. Patients with severe preeclampsia were given 10 mg. of reserpine intramuscularly or intravenously, and this dose was repeated in 1 or 2 hours if the patient was still hypertensive. Thereafter, 5 mg. was given every 4 to 6 hours as required to control the hypertension. Hydralazine was given intravenously in doses of 10 to 20 mg. as a single injection for a rapid initial blood pressure fall, if the desired response was not obtained with reserpine. This dose was repeated only when the normotensive state could not be maintained with reserpine alone. A continuous infusion of 40 to 50 mg. of hydralazine to 100 cc. of 10% dextrose in water was administered when the blood pressure was labile or when it was difficult to achieve the desired response. The basic therapy for eclampsia was 10 mg. of reserpine given intravenously and repeated in 1 or 2 hours if the patient was still hypertensive. This was followed with a maintenance dose of 5 to 10 mg. intramuscularly, every 4 to 6 hours, to insure sedation and normotension. Hydralazine, 20 mg. in a single intravenous injection, was also used if the blood pressure was 170/100 mm. Hg or above; if the blood pressure was between 150/90 and 170/100 mm. Hg only 10 mg. of the drug was given. If the blood pressure was lower, it was safer to give the drug more slowly by continuous intravenous drip, using only 35 mg. to 100 cc. of 10% dextrose in water. Supportive measures included administration of oxygen, fluid balance, diuretics, tracheotomy, bed rest, and sedation.

Of the 303 patients, 275 (91%) had a good response and 28 (9%) had a fair response. There was no poor response in the entire group. There was not a single maternal death from toxemia. Profound sedation was noted in 20 patients (6.6%) but was not harmful in any of these. Nasal congestion was observed in 36 patients (11%). Mild hypotension occurred in 3 patients (0.9%), oculogyric crisis in 3 (0.9%), and some tremor in 10 (3.3%). None of these side-effects was considered serious, and none persisted. The use of reserpine and hydralazine for effective, safe blood pressure control makes possible more rapid stabilization of the toxemia. This early stabilization allows earlier delivery in the seriously ill patients. A desirable amount of sedation is obtained as a side-effect of reserpine. The bradycardic effect of reserpine cancels the undesirable tachycardia due to hydralazine. Reserpine may be used more freely without the fear of the drastic fall in blood pressure associated with the use of veratrum and hydralazine. Maternal morbidity and mortality are decreased, and fetal salvage is increased by the use of this method. Reserpine alone, or in combination with hydralazine, offers the most effective, rational approach for control of blood pressure in patients with toxemia of pregnancy.

An Examination of Fertility of Women Following Pregnancy According to Height and Weight. T. McKeown and R. G. Record. Brit. J. Prev. Soc. Med. **11**:102-105 (April) 1957 [London].

The incidence of conception within 2 years after delivery of a previous child (20.8%) was used as an index of the fertility of 939 women. Fertility declined with age; the trend in association with parity was U-shaped, incidence of conception being lowest in women who had had 2 previous pregnancies.

The only evidence of association between fertility and weight was a low incidence of conception (11.1%) among the 73 women in the heaviest weight group (170 lb. [77.1 kg.] and over). The observed regression of weight on height was used to divide women into 5 groups according to body build. The data suggest that fertility is somewhat higher among women within 5% of the expected weight for height than in those above or below this level.

Healed Genital Tuberculosis: A New Etiologic Factor in Ectopic Pregnancy. I. Halbrecht. Obst. & Gynec. **10**:73-76 (July) 1957 [New York].

Of 100 women who received antibiotic treatment for latent genital tuberculosis, 20 conceived. Fourteen of these had a tubal pregnancy; only 6 had an intrauterine pregnancy and 3 of these ended in a miscarriage. The 3 miscarriages occurred in patients with endometrial tuberculosis, the more advanced form of female genital tuberculosis. Two of these patients were later operated on for tubal pregnancies. Any pregnancy occurring after antibiotic treatment of genital tuberculosis demands watchful supervision, considering the fact that such a pregnancy has, a priori, a 4-to-1 chance to be a tubal pregnancy or to end in miscarriage. This is especially true if the disease has reached the endometrial stage before the antibiotic treatment was started. Antibiotic treatment of genital tuberculosis is to be considered as a new causative factor in tubal pregnancy. Spontaneously healed tubal tuberculosis is probably much more common than is suspected and deserves more consideration as a causative factor in tubal pregnancy. The prevention of ectopic pregnancies resulting from antibiotic treatment of latent genital tuberculosis depends on the early detection of the disease when integral restitution of the tubal functions might still be expected. The only diagnostic means which has made possible detection of latent genital tuberculosis in its earliest stage is culture of the genital secretion and particularly of the menstrual discharge.

Intrafunicular Blood Transfusion for the Reanimation of Newborn Babies with Asphyxial Syncope. M. Marchesoni. Minerva ginec. **9**:423-429 (March 31) 1957 (In Italian) [Turin, Italy].

The author describes the method used in reanimation of 2 newborn babies with asphyxial syncope. Absolute apnea occurred in the first baby after 2 or 3 spasmodic inspirations. The heart stopped beating after 3 to 4 minutes of life. Intracardial injection of 0.5 cc. of adrenalin after aspiration of 2 or 3 cc. of blood had no effect. The child showed no signs of life and was thought to be dead. A plastic tube was introduced into the umbilical vein to a distance of 12 to 14 cm. until it reached the ascending vena cava. After the injection of 3 cc. of blood a fast, deep, and almost violent inspiration took place. Respiration and cardiac pulsation became normal after the introduction of 30 cc. of blood. The second baby presented absolute apnea at birth; heartbeats were irregular and few. An infusion of 50 cc. of blood through the umbilical vein was started 2 minutes after birth. The baby showed no signs of respiration during the transfusion, but the pulsations of the heart became more frequent. The first spontaneous inspiration, which was slow and superficial, came 15 minutes after birth. Respiration became almost normal 1 hour after birth. Administration of oxygen was continued, but the child did not cry, remained in coma, and died after 52 hours. The authors think that the success of reanimation by means of blood transfusion through the umbilical cord does not depend on the time within which it is possible to intervene but on the manner of onset and cause of the asphyxial syndrome.

PEDIATRICS

Outbreak of Aseptic Meningitis (Meningoencephalitis) with Rubelliform Rash: Toronto, 1956. R. A. Laforest, G. A. McNaughton, A. J. Beale and others. Canad. M. A. J. **77**:1-4 (July 1) 1957 [Toronto].

A study of 96 cases of aseptic meningitis suggested that 50% of the cases were caused by poliomyelitis, Coxsackie B, or Echo (enteric cytopathogenic human orphan) viruses. An outbreak of aseptic meningitis in 1956 was characterized by the appearance of a maculopapular rubelliform rash. This particular combination of aseptic meningitis and rash had not been observed in that area prior to the epidemic. During the summer of 1956, 115 children, 73 (63.4%) ranging in age from 5 to 9 years of age and none of whom exceeded 15 years of age, were admitted to the Hospital for Sick Children, Toronto, with a diagnosis of aseptic meningitis. A history of biphasic illness was obtained in 42 patients (36%), the main features of the first phase being fever, cold in he head, vomiting, diarrhea, and sore throat. It is of interest that the predominant clinical feature of those patients admitted in July was lethargy, while in those patients admitted in August and September irritability was found to be the prominent clinical feature. The most dramatic clinical manufestation was the appearance of a finely maculopapular rubelliform rash covering the face, trunk, and extremities in 50 patients (43%). No lesions were found in the throat, lymphadenopathy was not a feature, the rash did not scale and healed without complications, and the disorder occurred indiscriminately in those vaccinated or not vaccinated with Salk vaccine. No evidence of paralysis was found in any patient, recovery being

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for the most part uneventful. Nine strains were isolated from stools and 4 from cerebrospinal fluid, all of which were ether-resistant, produced paralysis in day-old suckling mice, and failed to be neutralized by antiserums to poliomyelitis virus save for Echo virus type 9. Differential diagnosis of this disease entity is hampered by the presence of this rash, as the clinical picture is similar to that found in other disorders, namely, rubella, meningococcemia, brucellosis, leptospirosis, and infectious mononucleosis.

To What Extent Have Antibiotics Influenced the Course of Pulmonary Tuberculosis in Children? F. Piéchaud and A. Morvan. Rev. tuberc., Paris **21**:256-261 (March) 1957 (In French) [Paris].

The records of 2 groups of children aged 8 months to 14 years with primary tuberculosis, one treated before 1947, when antibiotics came into use, and the other treated since then with various antibiotics, alone or in combination, were compared to determine the effect of antituberculous drug therapy on the course of the disease. Treatment in the first group, which contained 96 children, consisted of removing them from sources of massive infection and enabling them to live in circumstances in which they were provided with good conditions of hygiene, rest, and diet, under the influence of calcium and vitamins. Seven of the children in this group died and 1 was worse when he left the sanatorium than when he entered it; 11 who had had an average stay of 5 months were unimproved at the time of departure; 25 with an average stay of 10 months were improved; and 52 with an average stay of 21 months were cured. These figures show that the course of the disease was favorable only when the stay in the sanatorium was prolonged to an average of 18 months.

Treatment in the second group, which contained 68 children, began in 1947 with the use of streptomycin alone. The administration of aminosalicylic acid, given orally, was started in the second half of 1950, and 2 years later isoniazid was added. All 3 medicaments were given together at first, but before long streptomycin was reserved for severely affected patients, while the rest were given a combination of isoniazid and aminosalicylic acid. The results obtained in this group as a whole, without reference to the antituberculous drugs used, or the combinations in which they were given, were 39 children cured after an average stay of 24 months; 26 children improved at the time of departure after an average stay of 13 months; and 2 children unchanged as to their radiographic status at the end of 12 months; in addition, 1 child died during an operation. Treatment of 22 children with streptomycin and aminosalicylic acid was followed by improvement in 5 after 16 months and by cure in 17 after 31 months. The period of sanatorium care for 31 children treated with aminosalicylic acid and isoniazid, on the other hand, was slightly shorter: 13 months for 14 who left the sanatorium improved and 18 months for 17 who were cured.

One of the most significant advantages of antibiotic therapy lies in its ability to lessen the occurrence of local complications and to prevent the spread of the disease. Many of the children in the first group had suffered greatly from undernourishment during the second World War, and this may account in part for the fact that complications occurred in 10 and were severe enough to cause death in 7, but even so the difference between this group and the 2nd, in which there was only 1 complication, was striking.

Prolonged antibiotic therapy for patients with primary tuberculosis has been advocated by some authors and opposed by others. The question cannot be decisively answered at present, but the facts at hand seem fully to justify the use of antibiotics (1) in all children less than 3 years of age, in whom tuberculosis is admittedly dangerous; (2) in older children with severe infection first revealed by impairment of their general condition; (3) in all children with choroidal tubercles or gastric washings positive for tubercle bacilli; (4) in children with open lymph-node infection; and (5) in those with an x-ray picture of epituberculosis. Many phthisiologists and pediatricians believe that the manifestations of epituberculosis will disappear spontaneously and that rest in a sanatorium or even at home is all the treatment needed, but it is doubtful whether a complete cure can be obtained in this way, even in the most favorable cases.

Clinical Aspects, Diagnosis and Epidemiology of Herpes Simplex Infections. O. Vivell, W. H. Hitzig and H. J. Cremer. Helvet. paediat. acta **12**:127-146 (June) 1957 (In German) [Basel, Switzerland].

The authors discuss present-day concepts on the relationship between the human host and the herpes viruses, calling attention to the extensive studies on herpes antibodies carried out by Burnet and by Dodd and collaborators about 2 decades ago, which indicated that the primary infections with herpes virus are generally latent and become manifest chiefly in the conversion to positive of the serologic reactions. Human subjects seem to be the only reservoir of the herpes virus, but, since the infection is chronic, it is readily disseminated. Exogenous infection seems to play no part in those who have become immune, but despite this immunity to exogenous infections there are recurrent endogenous eruptions of herpes simplex. A diagram illustrates the relationship between the human host and the virus of herpes. The serums of 184 persons of various age groups were studied by means of complement fixation tests for the presence of herpes antibodies, and it was found that in the region (in

south Germany) in which these studies were carried out the percentage of persons with such antibodies increased with age.

At the age of 14, antibodies to herpes simplex virus were present in 84% of the persons examined. This shows that, as in case of other virus infections, the primary infection with herpes simplex takes place chiefly during childhood. Complement fixing antibodies are transmitted by the diaplacental route to newborn infants, who thereby acquire a certain passive protection against the dangerous exogenous infection that threaten during the first weeks of life. Primary infections with herpes, if they produce clinical symptoms, usually take a more serious and more prolonged course than do the more frequent and inoffensive recurrences. They are protean in their clinical manifestations; they may appear as aphthous stomatitis, herpetic vulvovaginitis, keratoconjunctivitis, herpetic eczema, inoculation herpes, meningoencephalitis not always recognizable as herpes, and a generally fatal herpes sepsis in the newborn infant. Primary herpes can be differentiated from recurrences by a rise in antibody titer during the convalescence in primary infection as against constant titers in recurrences. Serologic and some virologic studies were carried out on 14 patients with clinical signs of herpes. Three of the patients had recurrent herpes of the lips, 8 had stomatitis, 1 had herpetic eczema, in 1 a finger became inoculated with herpes as the result of sucking in the presence of herpes of the lips, and the meningoencephalitis in a young infant seemed to be of herpetic origin. The importance of the diagnostic studies for the etiological clarification of these disease entities is explained on the basis of detailed case histories.

A Case of Congenital Cancer. D. W. Beckett. East African M. J. 34:143-144 (April) 1957 [Nairobi].

The child reported on was born at home but was brought to the hospital 27 hours later because of a lump on the face. The child appeared to be a well-formed, full-term, living, male, newborn infant. There was a soft tissue tumor rising from the left cheek. This tumor was about the size of a tennis ball. It appeared to be nodulated and was fairly mobile. The covering skin was stretched thinly over it and was bluish-pink in color. The tumor was not pulsating. A provisional diagnosis was made of a congenital cyst, probably dermoid, and the child was kept in hospital for observation. During the next 6 days the infant's condition deteriorated. The tumor increased slightly in size, and the baby had a steadily increasing difficulty in taking its feedings. After 2 days it had to be fed on expressed breast milk with a spoon, and after another 2 days tube feeding was necessary. At operation the tumor was found to be obviously malignant. There was no differentiation at all, and the anatomy of the cheek was so distorted that none of the landmarks could be made out. The tumor appeared to be rising from the maxilla. The mass was removed with extreme difficulty, and at the end it was seen that the facial nerve and vessels had been destroyed. The operation was completed at 4 p. m. and the child died at 5:30 p. m. Permission for autopsy could not be obtained. Examination of the surgical specimen indicated that the tumor was a poorly differentiated neuroblastoma, possibly of the "retinal anlage" type.

First Results in the Therapeutic Use of Promazine in Children with Neuropsychiatric Disturbances. O. Vergani and E. Aldeghi. Minerva pediat. 9:467-470 (April 28) 1957 (In Italian) [Turin, Italy].

Treatment with promazine administered by mouth had a beneficial effect on 23 of 27 children, 5 to 13 years old, with neuropsychiatric disturbances. Twenty-two children were male and 5 female. Most of the children manifested psychomotor instability, irritability, reactivity, and impulsive aggressiveness; 13 had epilepsy. All children had an abnormal electroencephalogram. The average IQ of 18 children to whom it was possible to apply the Binet test was about 75. Each child received a dose of from 50 to 200 mg. of promazine per day (1.4 to 6 mg. per kilogram of body weight). The treatment was continued for more than 3 months in 19 children. The results were very good in 6 children, whose behavior returned to normal; good in 13 children, whose behavior improved to the extent that they could be safely dismissed from the institute; and fair in 4, who were also dismissed from the institute. The drug had no effect on 4 children. The results obtained in the 13 epileptic children were very good in 1, good in 10, and fair in 1; the drug had no effect in 1 child. The drug was well tolerated even when high doses were given. Drowsiness was not observed. The children who were dismissed were able to keep up their attendance in school. The children were again observed 1 month after the end of the treatment; very good results were still present in 4, good results in 7, fair results in 2, and no results in 14. The IQ of the children in whom the drug had very good results went up to 85.

Duodenal Enzymes in Infants with Kwashiorkor or with Dystrophic Condition. G. Russo and P. Buttitta. Minerva pediat. 9:382-392 (April 7) 1957 (In Italian) [Turin, Italy].

The authors report on the values of the duodenal enzymes in 3 groups of infants. The first group was composed of 8 children with domestic Kwashiorkor. The second group was composed of 12 infants with dystrophy; of these, 11 had hepatic steatosis, 5 riboflavin deficiency, 8 hypodysprotinemia, and 5 edema. The third group was composed of 12 normal

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children used as controls. The enzyme values were low in the duodenal juice of all the children with Kwashiorkor and in some of the children with dystrophy. The values were higher or became normal after the children had recovered from the disease. The authors believe that the pancreatic alteration that accompanies the deficiency of essential nutritive factors does not cause hepatic steatosis.

Changes in the Eyegrounds of Children with Diabetes. E. Heinsius. Deutsche med. Wchnschr. **82**:918-919 (June 7) 1957 (In German) [Stuttgart, Germany].

Retinal changes have become frequent in diabetic adults since their life expectancy has increased, but in diabetic children these changes were regarded as rare. The author studied the eyegrounds of children in a camp for diabetic children and found that 17 of 78 had retinal changes, such as punctate hemorrhages, capillary aneurysms, signs of earlier hemorrhages, whitish areas (indicative of capillary blockage) at the posterior pole of the retina, and irregularities in the venules, such as ampulla-like dilatations. Comparing these findings with those observed in older diabetic patients, they seem to be mostly characteristic of the early stages of diabetic retinopathy. In 5 of the children the macular reflex was abolished and pigmentation was somewhat reduced, changes that are observed only in older adults. The diabetic children ranged in age from 9 to 19 years, and in those with eyeground changes the diabetes had existed for from 4 to 8 years, whereas in most of those with normal eyegrounds the diabetes had been present for less than 4 years. On the basis of these observations the author regards it advisable to examine the eyegrounds of diabetic children at intervals of not longer than 4 years, and, if retinal changes are found, suitable treatment should be started at once. In view of the doubtful prognosis of diabetic retinopathy, the family physician or the pediatrician should give advice in selecting the occupation of these children.

Treatment of Toxoplasmosis During Childhood. H. Käser. Helvet. paediat. acta **12**:155-178 (June) 1957 (In German) [Basel, Switzerland].

The author presents observations on 5 children with toxoplasmosis, of whom 3 had antenatal and 2 had postnatal infection. Of the 3 children with the congenital form, one 5-month-old girl had signs of psychomotor retardation, hydrocephalus, and extensive, refractory chorioretinitis on the left side. A 10-month-old boy had psychomotor developmental deficiency, epileptiform fits, and bilateral optic atrophy with extensive, more recent chorioretinitis. An 8-year-old boy had increasing character changes, choreiform movements, tremor, and attacks of severe frontal headache with electroencephalographic changes indicative of essential epilepsy. The acquired form of toxoplasmosis manifested itself in a 2-year-old boy as acute encephalitis, and in a 3½-year-old girl it appeared with the signs of a postencephalitic state with severe psychomotor defects and epileptic convulsions. None of the children with toxoplasmosis showed intracerebral calcification.

Of the various drugs that have been tried in the treatment of experimental and of clinical toxoplasmosis, it appears that 2 groups of substances are especially promising. These are the sulfonamides, especially sulfapyrimidine, and pyrimethamine (a derivative of 2:4 diamino-pyrimidine). If these substances are given in combination they exert a synergistic effect. The combination Diazil (sulfamethazine)-Daraprim (pyrimethamine) was used in the 5 children with toxoplasmosis, and a therapeutic effect was observed in all. In 3 patients the Sabin-Feldman serum-dye test, as well as the complement-fixation reaction, became negative; in the other 2 patients the complement-fixation reaction became negative and the serum-dye test became so low that it may be expected to become negative. The clinical status greatly improved in 3 of the children, and in the other 2, except for slight persisting electroencephalographic changes, clinical and serologic cure could be obtained. Thus the efficacy of the combined sulfapyrimidine-pyrimethamine treatment has been proved in human subjects. Optimal dosage and period of treatment have not been definitely established.

DERMATOLOGY

Lichen Sclerosus et Atrophicus with Oral Involvement: Histopathologic Study and Dermabrasive Treatment. R. F. Miller. A. M. A. Arch. Dermat. **76**:43-55 (July) 1957 [Chicago].

The findings in 1 patient with bullous lichen sclerosus et atrophicus associated with vulval, perianal, and oral manifestations, are compared with those described in the literature. Lichen sclerosus et atrophicus is a morphologic entity. This has been established and based on a distinctive histopathological picture, most characteristically seen in older lesions. Early papular and macular lesions in the patient reported on have been found to be erythematous or brownish, apparently because of the presence of an infiltrate beneath the epidermis composed of lymphocytes, histiocytes, and fibroblasts. A narrow zone of homogenization was seen early in the disease, and the band-like or massive infiltrate was in apposition to the basal-cell layer. Lichen sclerosus et atrophicus is clearly differentiated from lichen planus by the different char-

acter of the early infiltrate and the further course of the histopathological changes. Degeneration, rarefaction, and destruction of elastic fibers are a histopathological feature of lichen sclerosus et atrophicus. Oral mucous membrane lesions with a histopathological appearance compatible with lichen sclerosus et atrophicus appeared to be a manifestation of this disease. Excellent results were obtained with the dermabrasive technique used as a form of therapy.

Lichen Sclerosus et Atrophicus of the Mouth. H. G. Ravitis and A. L. Welsh. A. M. A. Arch. Dermat. **76**:56-58 (July) 1957 [Chicago].

Three patients with lichen sclerosus et atrophicus involving the mucous membrane of the mouth are reported on. Lesions confined only to the mouth were found in one of these patients. This is an unusual feature which appears reported for the first time in the literature. Lichen sclerosus and atrophicus is not to be confused with localized scleroderma or lichen planus. The primary lesion of this disease, seen on the mucous membrane, is similar to that seen on the skin. It seems from these reports and other communications that lesions of lichen sclerosus et atrophicus of the mucous membranes of the mouth are not so rare as was formerly thought. In some patients the early lesions of the disease may appear on the oral mucous membranes.

Metastasizing Sweat-Gland Carcinoma: Report of a Case. H. A. Teloh, R. B. Balkin and J. P. Grier. A. M. A. Arch. Dermat. **76**:80-86 (July) 1957 [Chicago].

A 55-year-old female with a sweat-gland tumor of the foot of 18 years' duration presented a metastatic lesion to an inguinal lymph node 10 months after the excision of the primary tumor. Three previous admissions were recorded in 1937 and 1938 for paratonsillar abscess, septicemia, abscesses of the right thigh and left ankle, and empyema of the pleural cavity with drainage of the empyema and subsequent tonsillectomy. The patient first noted a small tumor on the plantar surface of the left foot in 1937, after removal of a cast applied for pyogenic arthritis of the left ankle. During the subsequent 18 years the nodule was asymptomatic, gradually increased in size, and was thought to be a lipoma. After a local excision, the major portion of the tumor presented the histologic appearance of a benign tumor of sweat-gland origin. One small area in the histological preparation showed atypical proliferation underlying the cystic epithelial lining with local invasion of the adjacent stroma. In this area there were marked nuclear membranes, clumping of chromatin, prominent nucleoli, nuclear pyknosis, karyorrhexis, and numerous mitoses, all generally accepted changes, sufficient for a histological diagnosis of cancer. The patient was next admitted to hospital in 1956 for a painful recurrent nodule in the scar of the previous excision. The lesion was excised and the pathological diagnosis was epidermal inclusion cyst of skin. No inguinal adenopathy was noted. The final admission occurred 6 months later, because of a slightly tender lump in the left femoral area. The metastatic lymph node lesion showed a picture similar to that of the tumor. It is, therefore, clear that the metastatic focus arose from the area of anaplasia in the primary tumor rather than from the well-differentiated and essentially benign portion making up the bulk of the tumor. The mass was excised and an inguinal lymph node dissection was done. The patient recovered without complications.

The acceptable cases of metastasizing tumors of sweat-gland origin are listed. Metastases to regional lymph nodes were almost invariably the first manifestation of spread of the tumor and occurred in 18 of 23 cases. In 12 cases the metastatic lesion was limited to regional lymph nodes. In 48% of the cases dissemination of metastases occurred and caused death.

Pacinian Neurofibroma. P. H. Prose, G. J. Gherardi and A. Coblenz. A. M. A. Arch. Dermat. **76**:65-68 (July) 1957 [Chicago].

A gradually enlarging, painful dermal growth with superficial ulceration in the heel of a 62-year-old man proved to be a Pacinian neurofibroma. Examination of histological sections showed no evidence of inflammation to explain the increase in size, since structures resembling immature Pacinian corpuscles were present in the depth of the tumor and others mimicking mature Pacinian corpuscles were seen in the superficial portion of the tumor. It is the author's belief that the tumor was growing in its deeper portion, perhaps by budding, and, while the immature corpuscles matured, they enlarged individually and occupied progressively more of the superficial part of the neoplasm. The tumor was excised, along with a wide margin of healthy skin and subcutaneous tissue. The family history and the physical examination of the patient did not reveal any evidence of neurofibromatosis.

Dermatitis Herpetiformis: Relatively Frequent Skin Disease in Norway. B. Langeland. Tidsskr. norske lægefor. **77**:380-381 (May 1) 1957 (In Norwegian) [Oslo].

Dermatitis herpetiformis occurs oftener in Norway than in the United States and England, is seen oftener in men than in women and most often in the age group between 20 and 60. The disease is chronic, but there is usually a regressive trend. The symptoms are aggravated by drugs containing iodine, by certain foodstuffs (particularly seafish),

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by mental stress, and by physical strain. For many years sulfapyridine and in more recent years Diasone have been used extensively as the only effective symptomatic agents. Long-continued application of these substances can lead to grave complications, and regular medical control is called for during their use. Of the 90 patients with the disease treated in the dermatological department of the Rikshospital from 1945 to 1950, 85 could be traced. Follow-up study showed that 8 were dead, 13 had recovered, and 64 were still suffering from the disease. The symptoms had shown a regressive trend in 51 cases and had continued unchanged in 13.

UROLOGY

Prostatic Adenocarcinoma (Medullary Type). C. G. Weller. J. Urol. 77:864-870 (June) 1957 [Baltimore].

Soft types of carcinoma of the prostate gland are uncommon. They are of importance chiefly because of the diagnostic difficulties which they present. Young divides the soft carcinomas into 3 types: (1) an infiltrating growth in which the cells, apparently growing faster than usual, collect in masses or separate the connective tissue and muscle fibers so much that no firm stroma is present (a picture which may be called medullary carcinoma); (2) glandular or tubular carcinoma in which the elements are close together, separated only by a minimal amount of stroma; and (3) large areas of intra-acinous proliferation where no stroma is present. The author presents observations on 3 patients with the medullary type of adenocarcinoma of the prostate, in the first of whom it was misdiagnosed preoperatively as benign prostatic hyperplasia. Suprapubic enucleation was attempted, but the tissue was so soft that it was removed with a gallbladder spoon in slightly yellow-white, waxy lobules of low vascularity resembling in consistency fresh pancreatic tissue. The second and third were approached transurethrally and cut like soft cheese with little bleeding.

The author emphasizes that the lesions here reported are variations of one kind of tumor, i. e., adenocarcinoma. This kind of prostatic cancer varies from the commonly encountered hard, nodular, fixed, slowly growing scirrhous type to the almost fluctuant, smooth, fungating medullary type, with all the gradations between these two extremes. The cellular structure of the medullary tumor is much less differentiated and presents a much more malignant microscopic picture than does the scirrhous type. Because of the very rapid proliferation in the medullary tumors, the tendency to formation of fibrous stroma is greatly reduced, causing the extreme softness of this type of adenocarcinoma. Probably because of its lesser degree of cell differentiation, the medullary tumor shows less tendency to elevate serum acid phosphatase levels. Theroetically, its resistance to estrogenic therapy may be due to decreased ability of estrogen to interfere with anaerobic respiration of the less differentiated cells of this type of neoplasm.

The Management of Wilms' Tumor as Determined by National Survey and a Review of the Literature. B. S. Abeshouse. J. Urol. 77:792-811 (June) 1957 [Baltimore].

The conclusions presented by Abeshouse are based on an analysis of the replies of 93 surgeons to a comprehensive questionnaire, an extensive review of the literature, and his own observations on 6 patients with embryoma of the kidney (Wilms' tumor). A study of the results obtained in 777 surgically treated patients revealed a low surgical mortality (2.7%), a high death rate during the first year after the operation (54.3%), and that relatively few patients survived 2 years or longer after the operation. A detailed study of 434 patients treated by 52 surgeons revealed that better results were obtained by preoperative irradiation plus nephrectomy and postoperative irradiation than by nephrectomy and postoperative irradiation, that is, the surgical mortality was 1.5% rather than 2%; the death rate during the first postoperative year was 50% rather than 54.8%; and the 2-year survival rate was 25.8% rather than 15.2%. A study of 212 cases reported in the literature between 1950 and 1955 also showed a somewhat higher 2-year survival rate in those treated by preoperative irradiation, nephrectomy, and postoperative irradiation (31.1% compared with 28%). The best results are obtained when the embryoma of the kidney is recognized during the first year of life.

The following factors are regarded as the advantages of preoperative irradiation: (1) the marked reduction in the size of the tumor renders the operation easier and safer in the moderate-sized tumors and feasible in the large or so-called inoperable tumors; (2) the changes induced by irradiation within the tumor reduce the likelihood of blood loss, tumor spread, metastases, and rupture during the operation; (3) during the course of the irradiation treatment the general condition of the patient may be improved by the use of antibiotics, transfusions, and the administration of fluids intravenously; (4) many urologic surgeons have found that the method reduced the surgical mortality and increased the survival rate. Postoperative irradiation has also gained wide acceptance, but the author warns against the indiscriminate use or irradiation as an adjunct to surgery. Irradiation is not without dangers, particularly when large doses are administered. Damage from radiation may involve the gastrointestinal, hematopoietic, osseous, pulmonary, and renal systems. Radiation nephritis is usually irreversible and may be fatal. Small operable tumors

require little or no irradiation. In patients with large tumors adequate doses of irradiation should be given within short periods to reduce the tumor to operable size, and the kidney should be promptly removed. The urologist is best qualified to assume the responsibility for the diagnosis and surgical treatment of embryoma of the kidney.

Intrarenal Aneurysm of the Renal Artery: Case Report. G. I. Smith and V. Erickson. J. Urol. **77**:814-820 (June) 1957 [Baltimore].

Only 115 cases of aneurysm of the renal artery had been reported up to 1951, and only 10 that originated in the intrarenal vessels. The authors present the history of a 43-year-old woman who had noted the sudden onset of dull, constant, right flank pain radiating to the right inguinal region and right thigh. This had persisted with some slight dysuria and frequency. She had had no hematuria, nausea, or fever. A similar episode had occurred 1 year previously but had subsided without treatment. The patient gave no history of trauma, passage of calculi, or urinary infection during her 6 normal pregnancies. Intravenous urograms revealed a pressure defect compressing the upper lower calyx with inferior displacement of the lowermost calyx of the right kidney. Retrograde pyelography confirmed the intravenous urographic findings. A translumbar aortogram resulted in immediate filling of a sac-like dilatation of a branch of the renal artery to the lower pole of the right kidney.

A diagnosis of probable intrarenal aneurysm was made and a right nephrectomy was performed through an 11th rib incision. Palpation of the kidney revealed no gross abnormality. When the kidney was halved, a 2.5-cm. cystic-appearing space having a vascular wall was encountered at the juncture of the lower and middle calyces. Since all vascular layers were present in its wall, this was, by definition, a true aneurysm. Because the remaining vascular system appeared normal, this may represent a congenital aneurysm developing at a vascular bifurcation.

The Results of 1,694 Consecutive Simple Perineal Prostatectomies. R. D. Turner and E. Belt. J. Urol. **77**:853-863 (June) 1957 [Baltimore].

The authors analyzed data on 1,694 patients who underwent simple perineal prostatectomy between 1930 and 1955. This report is concerned chiefly with the 1,613 patients in whom the microscopic examination revealed benign prostatic hyperplasia, the 81 who were found to have a malignancy of the prostate being omitted from further analysis. The authors preferred the perineal route because they believe that it involves less surgical and postoperative shock, thus permitting the surgeon the freedom to elect total removal if indicated by exploration or biopsy. They prefer a hypobaric spinal anesthetic, remove the Penrose drain within 24 hours, and permit the patient to be ambulatory. Dry heat is applied to the perineum twice daily beginning on the second postoperative day. The catheter is usually removed within 8 days and the patient discharged on the 9th day. Weekly postoperative visits are encouraged during the first 6 postoperative weeks. A total of 129 of the patients (8%) had undergone previous operations on the prostate, mostly transurethral resections. The authors cite data on urethral stricture and contracture of the neck of the bladder before and after the operation; on the incidence of other diseases of the genitourinary tract; on the classification into groups on the basis of the weight of the tissue removed; on incontinence; on sexual impotence; and on complications during and after surgery. The hospital mortality rate was 2.9%.

Simple perineal prostatectomy allows the surgeon an anatomically precise surgical approach. It is complicated by very little morbidity and mortality. It affords patients of the older age groups and those with cardiac defects a procedure involving a minimum amount of shock. This operation requires an average of 45 minutes. It is virtually free of operative and postoperative hemorrhage, a complication that adds to the morbidity in other forms of prostatic surgery. As with all types of surgery, the complications become less with experience. Simple perineal prostatectomy has a definite place in removing adenomas of all sizes and all pathological conditions. This operation has the advantage that it allows the surgeon to procure material for a rapid frozen section from capsular nodules suspected of being malignant. If prostatic cancer is found, the stage is set for total removal.

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OTOLARYNGOLOGY

Modern Treatment of Sinusitis. W. T. K. Bryan. A. M. A. Arch. Otolaryng. **65**:567-571 (June) 1957 [Chicago].

The sensitivity of the infecting bacteria to antibiotics, the allergic status, and the endocrine function, were studied to establish an accurate diagnosis of the etiological factors in 111 patients with sinusitis. Most of the patients were cured when these factors were attacked simultaneously and when appropriate drainage of blocked or filled sinuses was employed. One patient had polypectomy. All patients were given local medication to relieve congestion. Other medical treatment, given to 11 patients, consisted primarily in antibiotics and allergic management. Vaccines were used for patients with frequent acute infections without detectable defects, in those with prolonged and repeated courses of antibiotics, and in those with

bacterial hypersensitivity. Displacement was the reliable treatment of 59 patients during the subacute stage of the disease. Antrum irrigation was indicated for local therapy in 27, and both displacement and antrum irrigation were necessary in 10 patients. The remaining 3 underwent Caldwell-Luc operation. The "wiped nasal smear" offered objective cytological evidence in regard to the nasal mucous membrane.

Facial Rehabilitation Following Radical Parotid-Gland Surgery. J. J. Conley. A. M. A. Arch. Otolaryng. **66**:58-66 (July) 1957 [Chicago].

A lack of accurately coordinated knowledge concerning the microscopic classification of parotid tumors and their biology, management and prognosis, and the fear of injury to the facial nerve and the use of inadequate methods of facial rehabilitation are the main deterrents to the successful management of tumors of the parotid gland. The greater majority (70%) of the tumors can be cured without injury to the facial nerve. Of the remaining 30%, which are malignant tumors, the nerve need not be permanently damaged in treatment of this half of the group, leaving approximately 15 to 20% of the cases in which resection is indicated and rehabilitation is necessary. Should the tumor or cyst be confined to or occupy the major portion of the lateral lobe, a partial or total lateral lobectomy, respectively, in indicated. Faradic testing is not an absolute requirement in a partial lateral lobectomy but is used extensively in either total lateral lobectomy or total parotidectomy. Partial and total lateral lobectomy do not leave the patient with the facial nerve weakness due to trauma, stretching, and dissection along the nerve found in those patients who have experienced a total parotidectomy. Faradic testing admits of serious limitations, and only positive responses to such testing are considered, judgment being withheld on negative information until further evidence reveals itself in dissection. Small highly malignant tumors of the adenocarcinoma, squamous-cell carcinoma, mucoepidermoid carcinoma, and malignant mixed tumor types limited to the lateral side and not involving the facial nerve are treated by block dissection of the neck and total parotidectomy without permanent injury to the nerve. Should these highly malignant tumors invade the major portion of the lateral lobe or originate in the middle lobe or isthmus, it is usually impossible to salvage the facial nerve.

Five technical procedures are available to assist in the rehabilitation of the paralyzed face: (1) facial suspension, (2) muscle rotation, (3) facial balance, (4) nerve repair, and (5) nerve grafting. Facial suspension is probably the poorest approach to the problem of any of the techniques because the affected side of the face is completely paralyzed, devoid of all intrinsic muscle activity and appears normal only in an inert way in the position of repose. Muscle rotation (temporalis and masseter muscles) is valuable as an individual procedure and as an auxiliary to the nerve graft procedure. Facial balance is fairly simple, involving resection of 1 cm. of each of the muscle groups responsible for the exaggeration and imbalance of the normal side of the face. Should only the mandibular branch of the facial nerve be involved, facial balance is returned by resection of the same contralateral branch. Nerve repair is simple, direct, and affords the patient the maximum amount of facial rehabilitation in the shortest possible time. Nerve grafting has no appreciable advantage over nerve repair and has the disadvantage of impairing either tongue or shoulder function, and producing an aberrant type of muscle coordination. An active physiotherapeutic program is of inestimable value during the period of nerve regeneration. Galvanic stimulation, active bimanual massage of the cheek, heat, and active movement of the rotated masticatory muscle aid in maintenance of a high degree of muscle tone. Total regeneration of all of the nerve fibers is not necessary to produce good function, as a small percentage of fibers in the main trunk are capable of key connections in the peripheral apparatus.

Further Experience with Antimicrobial Therapy of Laryngeal Tuberculosis. L. J. Wallner. Eye, Ear, Nose & Throat Monthly **36**:397-400 (July) 1957 [Chicago].

As a consultant in otolaryngology at 2 large hospitals with 872 and 372 beds, respectively, for tuberculous male patients, the author had the opportunity to study for long intervals a large number of patients with laryngeal tuberculosis. Laryngeal tuberculosis is always secondary to pulmonary tuberculosis, and antimicrobial therapy administered for the pulmonary tuberculosis relieves or cures the laryngeal tuberculosis. Because tubercle bacilli develop resistance to the drugs under certain circumstances, 3 important principles must be followed to obtain optimum results. At least 2 of the antituberculous drugs must be given simultaneously; the drugs should be given continuously, and their administration should not be interrupted throughout the entire period of treatment. The therapy should be continued for many months or even years. The regimen most commonly used consists of 100 mg. of isoniazid 3 times daily and 5 Gm. of aminosalicylic acid sodium 3 times daily, or 100 mg. of isoniazid 3 times daily and 1 Gm. of streptomycin intramuscularly 2 times per week. Viomycin can be given with relative safety in doses of 1 or 2 Gm. intramuscularly 2 times per week.

These potent bacteriostatic agents are capable of ameliorating tuberculous laryngitis to such a degree that the laryngeal disease is no menace to the patient. Pain is completely relieved, the voice is restored, and the pathological alterations heal completely or to a marked degree and remain inactive. The patient's prognosis becomes related to his chest disease alone. Antimicrobial therapy of tuberculous laryngitis is so highly effective that most other measures are unnecessary. This includes complete voice rest, local medication, heliotherapy, cautery, and section of the superior laryngeal nerve. As more patients with tuberculosis are detected earlier and are given long continued chemotherapy, there should be a further decrease in the incidence of laryngeal tuberculosis. In a 12-month period beginning in April, 1955, 17 new cases of tuberculous laryngitis were detected among 2,005 patients newly admitted to the tuberculosis hospital. For comparison, in a 12-month interval in 1948 63 new cases of tuberculosis of the larynx were detected among 1,414 patients admitted to the hospital. Healing of the laryngeal lesions is not dependent on corresponding amelioration of pulmonary tuberculosis or improvement in the patient's physical state. Biopsy studies of prominent laryngeal lesions before the institution of chemotherapy and after antimicrobial therapy confirmed microscopically the healing that was evident on gross examination. The sequence of events seemed to be as follows: disappearance of tubercle bacilli, diminution of inflammation, disappearance of tubercles, and finally replacement of necrotic material by fibrous connective tissue. Healing was not dependent on this fibrous proliferation.

THERAPEUTICS

Clinical Experience with the Therapeutic Effect of a Sulfonamide-Sulfone Combination. A. G. Dettori and G. Salvi. Minerva med. **48**:1781-1787 (May 19) 1957 (In Italian) [Turin, Italy].

Forty-two patients with different forms of infection were treated with a sulfonamide-sulfone combination. The drug was prepared by combining sulfomethazine, sulfodiazine, and sulfone N-acetate in a 2:2:1 proportion. The patients received an average dose of 3 Gm. per day, 0.75 Gm. every 6 hours. The drug was administered in cycles of 7 to 10 days. Some patients received a beginning dose of up to 5 Gm. of the drug per day, others were subjected to a prolonged therapy for longer than a month and received an average dose of 2 Gm. per day. The drug was tolerated well by all patients. Untoward side-effects were not noticed. The drug had a very good effect on 19 patients with infections in the respiratory tract. Immediate remission of the symptoms occurred in patients with bronchitis and pneumonia; fever disappeared within 2 to 4 days in patients with parapneumonic pleural effusion; cough was checked markedly; and fever disappeared in patients with bronchiectasic and chronic forms of infection. Total remission of the symptoms and of the fever with diminution and reduction of the abscess cavity was obtained in a 42-year-old man with pulmonary abscess. The drug had a good effect on some patients who had derived little or no benefit from treatment with antibiotics. The drug had a partially beneficial effect on 15 patients with infection in the urinary tract. The subjective symptoms improved, but fever and the pathological urinary condition persisted. Antibiotics had to be used for the complete resolution of the symptoms. The drug had a beneficial effect on some patients with infection in the urinary tract who were operated on. The postoperative period was markedly shortened, and there was no fever. The drug had little or no effect on patients with localized infection (gluteal abscess) and in a patient with extensive thrombophlebitis. The drug, administered in fractioned doses and for a prolonged period of time, had a good effect in the treatment of micrococcic (staphylococcic) infections of patients with rheumatic fever.

Preludin Treatment of Obesity in Diabetes Mellitus: Preliminary Report. R. Robillard. Canad. M. A. J. **76**:938-940 (June 1) 1957 [Toronto].

Phenmetrazine (Preludin) hydrochloride was given a double-blind trial in 24 obese patients with diabetes mellitus. Two sets of tablets, which looked and tasted identically and which were distinguished only by the code of letters AZ and BY, were supplied. One set contained the active ingredient phenmetrazine, and the other was a placebo. The clinical investigator and the patients were unaware which tablet contained the active ingredient. As the study progressed, it was found that the BY tablets had no therapeutic effect, while the AZ tablets exerted a therapeutic effect. It was later confirmed that the BY tablets were the placebos.

The action of phenmetrazine then was studied in 51 obese patients between the ages of 16 and 74 years with diabetes mellitus, who were given 25 mg. of the drug 3 times a day, 1 hour before meals, for periods of from 2 to 26 weeks. An average reduction in weight of 1.01 lb. (0.5 kg.) per week was observed. Thirty-one of the 51 patients had had to take insulin, but 5 of the 31 improved to the extent of being able to discontinue taking insulin. Ten of the 31 patients were able to reduce the dose of insulin, and the average reduction was 13.2 units. The average weight loss was 0.8 lb. (36 Gm.). Sixteen of the 31 patients had to continue their treatment of insulin with the same dosage, but in these patients the average loss in weight was only 0.56 lb. (25 Gm.). The with-

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drawal or reduction in dosage of insulin thus was directly related to the degree of weight loss. While previous attempts at weight reduction with other drugs had failed in these obese patients with diabetes mellitus, they were benefited by phenmetrazine, which proved to be free of toxic effects. It did not aggravate the hypertension frequently observed in diabetic patients of a certain age, and it did not even produce palpitation. Phenmetrazine by its anorexic action will be of great help in the treatment of diabetes mellitus.

First Experiences with a New Malonilurea Derivative with Ganglion-Blocking Effect: 1,3-Bis-(β-trimethylaminoethyl)-5, 5 diethyl-malonilurea. G. Mininni. Sett. med **45**:59-62 (Jan. 31) 1957 (In Italian) [Florence, Italy].

The author reports on the results obtained in 128 patients treated with a new malonilurea derivative, C. S. 23, which has a ganglion blocking effect. One hundred patients, 20 normotensive and 80 with hypertension, received fractionated doses of from 5 to 50 mg. active ion of the drug intramuscularly and 30 to 60 mg. by mouth. Twenty-eight patients, 20 with hypertension and 8 normotensive, received a single dose of 30 to 60 mg. of the drug by mouth. Intramuscular administration of a dose of 5 to 45 mg. of the drug always caused a drop of the systolic and diastolic pressures. The best hypotensive effect and the best tolerance were obtained with a dose of from 25 to 30 mg. of the drug. The drop in blood pressure was more marked in patients with essential hypertension. The drug did not have a hypotensive effect in patients with primary or secondary kidney lesions. The drop of the blood pressure was gradual. The lowest reading was obtained 30 minutes after the parenteral administration of the drug. The effect of a dose of 25 to 30 mg. lasted 8 hours. The drug did not cause orthostatic hypotension. The author believes that the drug has its main effect on the orthosympathetic ganglia. Toxic phenomena and disturbances of the central nervous system, of the respiratory system, and of the heart were not noticed. Compared with hexamethonium, C. S. 23 is less habit-forming, is less toxic, and has a longer-lasting hypotensive effect.

Long Term Anticoagulant Therapy. J. H. Olwin and O. Paul. Surg. Gynec. & Obst. **105**:61-68 (July) 1957 [Chicago].

The fundamental principle of anticoagulant therapy is a cautious interference with the coagulative mechanism. The more favorable aspects of such interference are prevention of the formation of a thrombus, limitation of its extension once formed, and the recanalizing influence of at least one of the prothrombin depressants. Myocardial infarction as a complication of coronary disease is invariably due to thrombotic occlusion at the site of plaque formation. The fact that gradual mere narrowing of the coronary artery tree without thrombotic occlusion permits compensatory collateral circulation sufficient to provide adequate myocardial oxygenation is sufficient reason to attempt modification of coronary disease to prevent thrombotic coronary arterial occlusion by means of anticoagulants. Only those patients receiving a minimum of 6 months of uninterrupted anticoagulant therapy and having prothrombin levels less than 30% during the total period of treatment were included. No patient received either long-term heparin treatment or 2 long-acting anticoagulants simultaneously. The indications for use of long-term anticoagulants in this series are myocardial infarction, thrombophlebitis, real or threatened retinal vein occlusion, peripheral arterial embolism, peripheral arteriosclerosis, retinal atherosclerosis, cerebral thrombosis, and pulmonary embolism. The contraindications to anticoagulant therapy adhered to are blood disease with bleeding tendencies, severe hepatic disease, and severe renal disease. Factors influencing the control of anticoagulants are the physical status, intelligence, and cooperativeness of the patient; laboratory methods of control; properties and characteristics of the various anticoagulants; other drugs and agents administered during anticoagulant therapy; and the experience of the attending physician with anticoagulant therapy. Bleeding was the most frequent complication in this series, 4 episodes of gross hematuria occurring in 3 patients when the 2-stage prothrombin level was less than 10%. Only 2 of the 70 cases treated had a fatal outcome, and 1 of the fatalities occurred when the patient failed to return for routine prothrombin determination. Since safety is the prime consideration in long-term anticoagulant therapy, there are 2 requirements that must be satisfied: the physician himself must be familiar with the characteristics of complications from and with antidotes to the use of such agents or have proper professional guidance, and, secondly, a laboratory must be available which can perform consistently reliable prothrombin determinations. The risk of hemorrhage accompanying excessive anticoagulant effect is considerably less than that due to failure to maintain adequate depression of prothrombin level.

Anticoagulant Therapy in 521 Patients with Acute Myocardial Infarction. R. Armas Cruz, G. Lobo-Parga, S. Manubens Leiva and others. Rev. méd. Chile **85**:49-60 (Feb.) 1957 (In Spanish) [Santiago].

The authors used anticoagulant therapy in 521 patients with acute myocardial infarction, of whom 153 were hospitalized. Thirty-six patients were observed who received no anticoagulants. Treatment was started with heparin. For maintenance treatment the authors used bishydroxycoumarin

(Dicumarol) and phenindione. They preferred bishydroxycoumarin to phenindione because of its easier administration and better response. Phenindione may cause agranulocytosis. The ratio of males to females with acute myocardial infarction was 2.4 to 1. The mortality rate was 7.5% (39 deaths), and thromboembolism occurred in 2.3% of the patients. Mortality was higher among the patients not treated with anticoagulants. The preceding data do not include deaths which occurred within 48 hours after the beginning of the therapy, because the effect of bishydroxycoumarin is evident only after 48 to 72 hours. Hemorrhagic and other complications of this therapy were rare. Hemorrhage occurred in 28 patients (24 minor, 4 serious). The various types of hemorrhage, in order of importance, were ecchymoses, hemorrhoidal bleeding, and gingival bleeding. The authors recommend anticoagulant maintenance treatment for prevention of new coronary thrombosis and for treatment of repeated severe infarctions and persistent angina. This therapy requires the cooperation of the patient and his family.

Treatment of Radiation Lesions with Pancreatic Enzymes. A. Bacchi and A. Volta. Rass. clin. terap. **56:**107-117 (April-May-June) 1957 (In Italian) [Rome].

Treatment with proteolytic enzymes of pancreatic origin was beneficial in 4 patients with various radiologic lesions. The exudate was diminished and assumed a pinkish color, indicating a reactivation of circulation. One topical application was sufficient to obtain fast healing in 1 patient with an extensive recent lesion. The enzymes have a direct effect on the cicatrization process; best effects are obtained with an early treatment. Local improvement had a good effect on the general condition of one patient with a very severe lesion. The enzymes were administered intramuscularly in this patient. Improvement of the trophism of the periulcerous tissues, a progressive detergent effect on the focus, elimination of the necrotic parts, and a marked stimulation of the tissues of the healing process were observed. The lytic effect of the enzymes did not diminish in patients subjected to prolonged treatment.

Choice of Antibiotics for Treatment of Infections of Strictly Anaerobic Bacteria. E. de Lavergne, J. C. Burdin and J. Schmitt. Presse Méd. **65:**1054-1055 (June 5) 1957 (In French) [Paris].

The effects of antibiotics on strictly anaerobic bacteria are much less known than those on aerobic bacteria. For a long time, treatment of infections by anaerobic bacteria, except those of tetanus and botulism, was based on serum therapy. The advent of sulfonamides improved the results. The effect of sulfonamides is uncertain in infections due to strictly anaerobic bacteria. Penicillin has a powerful effect in infections caused by anaerobic bacteria. Streptomycin and neomycin have only a mild effect. There is a stronger effect with the tetracyclines and chloromycetin. There is very little knowledge as to the effect of Framycetin and Spiramycin. The authors studied the effect of 11 antibiotics on 17 species of strictly anaerobic bacteria. They suggest that penicillin be given in combination with chloromycetin or tetracycline in the early stage of the infection. At a later stage, when the laboratory has isolated and identified the various strains and determined their antibiograms, the clinician may adhere to his former choice or modify it by resorting to other antibiotics, such as erythromycin or Spiramycin, both of which are effective in infections with gram-positive bacteria. Streptomycin, neomycin, and Framycetin have little if any effect on infections by strictly anaerobic bacteria.

Gastrointestinal Side-effects Related to Prednisone and Prednisolone. J. R. Dordick, S. L. Felder, F. Polansky and A. Geffen. New York J. Med. **57:**2049-2054 (June 15) 1957 [New York].

Predisone and prednisolone have been established as effective antirheumatic and anti-inflammatory agents in a variety of diseases. Administration of these hormones in therapeutic doses is not usually associated with significant alterations in electrolyte and water metabolism, in contradistinction to administration of cortisone, hydrocortisone, and fluorohydrocortisone. Patients selected for this study were questioned as to whether they had experienced any gastrointestinal symptoms such as abdominal pain or discomfort, pyrosis, bloating, regurgitation, nausea, vomiting, diarrhea, or bloody or tarry stools. Definitive radiologic diagnosis of ulcer was based on the finding of a crater and/or constant deformity. Undesirable gastrointestinal side-effects were present in 35 patients (17.9%). Therapy was successful in 30 of these patients (15.3%) despite these side-effects, but medication had to be discontinued in 5 (2.5%). The presence of an active ulcer suspected clinically and particularly if confirmed radiologically is a contraindication to the use of these drugs. The presence of a chronic ulcer represents an unpredictable hazard, since activation, bleeding, or perforation may abruptly intervene in patients receiving prednisone or prednisolone without premonitory or clinical symptoms of an ulcer.

Myasthenic Crisis: Therapeutic Use of d-Tubocurarine. H. C. Churchill-Davidson and A. T. Richardson. Lancet **1:**1221-1224 (June 15) 1957 [London].

The authors present the history of a 56-year-old woman with myasthenia gravis who had undergone thymectomy and who gradually responded less and

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less to neostigmine. Various anticholinesterases were tried, but the patient finally collapsed, apparently from excessive drug therapy. Complete withdrawal of all neostigmine-like drugs for 7 days led, on resumption of therapy, to much improvement. This, however, was maintained for only a few days before severe myasthenia again became evident. Large doses of d-tubocurarine, which provided complete rest for the motor end-plates, led to a dramatic improvement, which was sustained with the aid of reduced neostigmine therapy for nearly 3 months.

Discussing the implications underlying this form of treatment the authors point out that the action of neostigmine at the motor end-plate has not been fully established. Its therapeutic value in myasthenia is generally attributed largely to its anticholinesterase properties, but this may not be the sole reason for it. The variability in response to neostigmine, not only in different patients but also in the same patient at different times, is characteristic of the disease. The altered response of the motor end-plates might be explained by an alteration in the ratio of acetylcholine molecules to those of choline, the former producing depolarization during their fleeting life-span and the latter persisting indefinitely and producing a nondepolarization block like that of d-tubocurarine. This may help to explain why myasthenic muscle which ceases to respond to neostigmine can be made to respond again if the neostigmine is withheld for a while. The present case illustrates this point.

The fact that the periods of rest were followed by improvement in the response to anticholinesterase therapy led to the next logical step—an even more efficient method of resting the motor end-plates. The authors assumed that the presence of a high concentration of a muscle relaxant, e. g., d-tubocurarine, would so raise the excitation threshold of the motor end-plate that the concentration of acetylcholine ions would be insufficient to cause stimulation. Thus the motor end-plate would enjoy a period of complete rest. This hypothesis was the basis for trying what might otherwise be described as dangerous treatment, namely, the giving of large doses of d-tubocurarine to a myasthenic patient. The results justified the attempt.

PATHOLOGY

Multiple Endocrine Tumors and Peptic Ulcer. E. R. Fisher and R. H. Flandreau. Gastroenterology **32**:1075-1094 (June) 1957 [Baltimore].

A patient with multiple ulcers of the duodenum and jejunum associated with hyperplasia of the parathyroids, adrenal cortices, amphophils and basophils of the anterior pituitary, and alpha cell tumors of the islets of Langerhans and heterotopic pancreatic tissues is presented. The initial symptoms were referable to hyperparathyroidism rather than to ulcer. The demonstration of glucagon or a biologically similar material in the serum indicated that the pancreatic tumors were functioning. The etiology of the peptic ulcers in patients with multiple endocrine neoplasms has not been adequately explained. The secretion of glucagon from the alpha cell tumors of the pancreatic islets may have a causal effect in the ulceration in such patients, since removal of such neoplasms has been followed by clinical remission. There is, however, little experimental evidence to indicate that glucagon possesses a direct ulcerogenic effect. It cannot be stated with certainty that the adrenal cortical hyperplasia and adenomas observed in this syndrome are the result of the secretion of glucagon. There is pathological evidence that the pituitary may play a role in the pathogenesis of these adrenal and other endocrine changes. Also the ulcerogenic effect of adrenocorticosteroid secretion merits consideration as a possible pathogenic factor of such lesions in this syndrome. There appears to be a more than fortuitous association between hyperparathyroidism and peptic ulcer. It was found that 24% of patients with hyperparathyroidism at the Mayo clinic had a peptic ulcer, and in some of these patients the ulcers were located in the jejunum. The exact mechanism of ulcer formation in patients with hyperparathyroidism has not been elucidated. Significant clinical and some experimental evidence appears to indicate that the peptic ulcers encountered in patients with multiple endocrine neoplasms may have a complex etiology involving parathyroid and adrenal cortical secretions, as well as perhaps an indirect effect resulting from the secretion of glucagon from islet cell tumors of the alpha cell type. The role of amphophilic hyperplasia of the anterior pituitary in the pathogenesis of multiple endocrine tumors encountered in patients with this syndrome is pointed out. It merits consideration that the hyperplasia might result from a deficiency of a target organ, such as testicular atrophy, as noted in the presented patient.

Multiple Gastric Cancers: Review of the Literature and Study of 42 Cases. C. G. Moertel, A. Bargen and E. H. Soule. Gastroenterology. **32**:1095-1103 (June) 1957 [Baltimore].

The pathological findings in 1,835 patients with gastric cancer diagnosed at the time of gastrectomy or from autopsy specimens in a 10-year period were reviewed. A total of 40 patients (2.2%) with tumors of unequivocal malignancy were confirmed as having multiple simultaneous gastric cancers. These were 34 men and 6 women; the lesions were verified at gastrectomy in 37 and at autopsy in 3. The average age at diagnosis in the men was 62 years, in the women 54 years; the range of age was from 40 to 81 years. Multiple adenocarcinomas were

found in 38 patients. Of these, 29 had 2 lesions and 9 had 3 lesions; 26 of these patients had tumors of different grades of malignancy and 12 had tumors of the same grade. In addition to these patients, one patient had 2 independent leiomyosarcomas and another had simultaneous adenocarcinoma and leiomyosarcoma. Three of the patients also had pernicious anemia and 4 had associated gastric polyposis. Two additional patients were proved to have one or more malignant neoplasms entirely independent of their multiple gastric lesions. One patient had a squamous cell carcinoma of the nasopharynx, 4 years after gastrectomy for multiple adenocarcinomas. The other had a preceding carcinoma of the sigmoid and a simultaneous hypernephroma of the kidney. The fact that 2.2% of the gastric cancers in this series were grossly multicentric and that 22% in another series were microscopically multicentric appears to give ample evidence for the assumption that a significant proportion of gastric carcinomas would present multicentric zones of malignant change at some stage in their development.

The Syndrome of the Metastasizing Pancreatic Adenoma with Exocrine Secretion. M. Schmid. Ztschr. klin. Med. **154:**439-455 (No. 5) 1957 (In German) [Berlin].

Secreting tumors of the exocrine tissues of the pancreas are rare, but they produce a typical syndrome, which is characterized by the triad of polyarthritis, panniculitis (of the Weber-Christian type), and blood eosinophilia. The pathological process underlying this syndrome is a metastasizing exocrine pancreatic adenoma, which, because of its structure, has been referred to as acinous-cell carcinoma. The author cites the history of a 71-year-old man who presented all the characteristic clinical and pathological aspects of the pancreatic adenoma with exocrine secretion. The tumor had a distinct structural and cellular picture, which, with its acinus structure, recalled the exocrine tissue of the pancreas, but differed from it by the absence of centroacinar cells and of excretory ducts. The malignant character was evident chiefly in the formation of distant metastases and in the occasional accumulation of atypical mitoses. For this reason and in analogy to the metastasizing adenoma of the thyroid the author prefers the term metastasizing exocrine adenoma of the pancreas. Metastases generally spread by way of the blood stream into the liver and, in some cases, selectively into the large fat depots: the subcutaneous tissues, the paraarticular fat tissues, and into the fat marrow of the long bones.

The tumor tissue secretes lipase and in this way produces extensive necroses in the fat tissues. These necroses develop either by the humoral route by passage of lipase into the blood and lymph channels from the primary tumor or the liver metastasis, or locally by lipase secretion from the tumor metastasizing in the fatty tissue. In the case presented it was possible to prove the secretion of lipases by the tumor tissue. The necroses in the fat tissues were produced by secreting metastases in the subcutaneous tissue in the para-articular fat tissue and in the fat marrow of the long tubular bones.

Genetic, Developmental and Hormonal Aspects of Gonadal Dysgenesis and Sex Inversion in Man. E. Witschi, W. O. Nelson and S. J. Segal. J. Clin. Endocrinol. **17:**737-753 (June) 1957 [Springfield, Ill.].

Studies on the causation of sex abnormalities involving sex inversions in man led the authors to recognize 3 definite classes, differing in causation, time of onset of manifestation in ontogenesis, and characteristic type of adult expression. Class 1 abnormalities originate from primary dysgenesis of the primordial germ cells—itself a consequence of damage to egg or free blastocyst (blastophthoria). In the case of complete disappearance of primordial goniums preceding the period of gonadal sex differentiation, genetic males become pseudofemales. If the number of goniums is only substantially reduced, genetic females develop into either pseudomales or true hermaphrodites. Class 2 abnormalities depend on a hereditary peculiarity of mothers, i. e., some agent which passes from the mother to the fetus counteracts the normal medullary functions of the fetal testes immediately following their embryonic differentiation. Hence, genetically male fetuses develop into male pseudohermaphrodites. Class 3 abnormalities develop as a sequel to adrenal hyperplasia, with production of androgenic hormones. Manifestation begins only in the 5th month or later. Genetically female individuals develop into female pseudohermaphrodites.

Sex Chromatin Pattern in Seminiferous Tubule Dysgenesis and Other Testicular Disorders: Relationship to True Hermaphrodism and to Klinefelter's Syndrome, with a Review of Gonadal Ontogenesis. M. M. Grumbach, W. A. Blanc and E. T. Engle. J. Clin. Endocrinol. **17:**703-736 (June) 1957 [Springfield, Ill.].

The chromosomal sex pattern was determined in 65 phenotypic male patients with testicular disorders who presented with either sterility, eunuchoidism, cryptorchidism, atrophic testes, or signs of Klinefelter's syndrome. Testicular biopsy specimens were obtained from all but 1 patient. Among these 65 patients, 9 with tubular fibrosis or germinal aplasia of the testis were found to have a female chromatin pattern. In these patients the chromosomal sex and the testicular histopathological structure indicated a gonadal disorder of a congenital nature for which the term "seminiferous tubule

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dysgenesis" has been proposed by the authors. A group of 23 chromosomal males with similar pathological and clinical findings have also been included in this category. Klinefelter's syndrome was a manifestation of this condition in some patients; however, not all patients with Klinefelter's syndrome had seminiferous tubule dysgenesis. The disorder was familial in 2 patients. One patient had myotonia dystrophica.

Present knowledge of gonadal ontogenesis in vertebrates was reviewed, particularly in placental mammals. In the light of animal experiments, the failure of the embryonic gonad to differentiate as an ovary in chromosomal females with seminiferous tubule dysgenesis has been attributed to a severe corticomedullary imbalance with complete suppression of the cortical component (ovarian primordium). As a result, the embryonic gonad is transformed into a testis capable of bringing about male sex differentiation. The evidence, though inconclusive, suggests that seminiferous tubule dysgenesis is a genetically determined disorder. Seminiferous tubule dysgenesis in chromosomal females appears to be the first example of complete sex reversal in the human. According to the concept presented, these persons may be regarded as a variant of classic true hermaphroditism because of the discrepancy between chromosomal and gonadal sex and in view of the mechanism of gonadal inversion. A concept of true hermaphroditism is proposed based on varying degrees of corticomedullary imbalance of the embryonic gonad.

Cytological diagnosis of sex should become a routine part of the study of testicular histopathology. Detection of a female chromatin pattern in phenotypic males is presumptive evidence of seminiferous tubule dysgenesis, provided true hermaphroditism and rare forms of female pseudohermaphrodism can be excluded. A male chromatin pattern in patients with primary testicular disorders does not rule out the diagnosis; in these patients it must be based on the testicular pathological picture. Determination of the cytological sex of boys with unusually small or firm testes, with cryptorchidism (unilateral or bilateral), or with adolescent gynecomastia should lead to the discovery of prepuberal cases and provide the opportunity to study the testicular lesion in this disorder at an early age.

RADIOLOGY

Idiopathic Hypercalcemia. J. A. Shiers, E. B. D. Neuhauser and J. R. Bowman. Am. J. Roentgenol. **78**:19-29 (July) 1957 [Springfield, Ill.].

The authors describe 4 cases of idiopathic hypercalcemia in 2 boys aged 2½ and 2 years and in 2 girls aged 17 months and 4 years and 8 months, the latter of these 2 also being a cretin. The first patient died of uremia, and autopsy was refused. The other 3 are living. The clinical features of idiopathic hypercalcemia may be attributed to the raised serum calcium level, to changes in organs damaged by prolonged hypercalcemia, and probably to associated abnormalities. The typical "elfin" facies, the muscular weakness, anorexia, vomiting, constipation, and failure to thrive associated with mental retardation and deterioration may suggest the diagnosis. The roentgen features of widespread osteosclerosis, evidence of defective bone formation, and abnormal soft tissue calcifications may be characteristic and should not be confused with those of any other entity. Amorphous increase in density of the skull and epiphyses, transverse bands of increased density at the ends of the bones, faulty tubulation, and deposit of calcium particularly in the kidneys distinguish this condition from other metabolic diseases. The causation is unknown, but the most likely cause is considered to be hypersensitivity to vitamin D.

The Familial Occurrence of Pulmonary Alveolar Microlithiasis. M. C. Sosman, G. D. Dodd, W. D. Jones and G. U. Pillmore. Am. J. Roentgenol. **77**:947-1012 (June) 1957 [Springfield, Ill.].

While in charge of the radiologic section of the Boston induction board, one of the authors saw a chest roentgenogram of a 45-year-old man showing both lungs filled by a fine sand-like mottling, resembling a snowstorm. There was no similarity to miliary tuberculosis or to any of the so-called miliary conditions previously seen and nothing to suggest either healed fungus infection or silicosis. The patient was free from symptoms, gave no history of occupational exposure, and showed completely normal responses to physical examination of his heart and lungs. This peculiar appearance in his chest roentgenograms had been known for about 5 years preceding 1942, but no one could make a definitive diagnosis or suggest a better name than the descriptive one of "pulmonary calcinosis." After several years of a completely symptom-free period, this patient gradually became dyspneic on exertion and eventually died following extreme pulmonary disability. The authors demonstrate in an extensive review that the condition is not as rare as it has been thought to be. It has also been designated as pulmonary alveolar microlithiasis. They found 21 cases reported in the literature, and they personally know of 25 or more unpublished cases, of which 23 are presented in this paper.

The etiology is unknown, but the high incidence of familial occurrence strongly suggest a hereditary factor. Thirteen of the 23 new patients were members of 5 families. The condition could be due to an inborn error of respiratory metabolism at the alveolar interface, possibly an enzyme fault. Calcium salts are more soluble in acid mediums and are more easily precipitated from alkaline solutions. Any-

thing which promotes alkalinity at the alveolar interface where oxygen and carbon dioxide are exchanged would promote the deposition or precipitation of calcium phosphate or carbonate. However, the problem of calcium deposition in tissues is not germane to the problem, as the deposit is not in tissue but in an exudate or transudate in an otherwise presumably normal alveolus. Injuries to the alveolar walls could cause the exudate, but the real problem, still to be solved, is what causes the deposit of calcium phosphate and carbonate in the exudate. Another suggestion is that the formation of the microlith is due to an abnormality of carbonic anhydrase, which plays an important part in the exchange of oxygen and carbon dioxide and probably also in maintaining normal balances between the extremes of acidity and alkalinity. The enzyme could be deficient, in excess, or abnormal in function. Given an exudate in the alveoli which under normal conditions would be absorbed, the presence of some organic material normally found only in calcifying tissues or ossifying bone might lead to calcium precipitates. The disease usually is asymptomatic for years. It is generally discovered by chest roentgenography. Overexposed or overpenetrated films are necessary to demonstrate the fine sand-like particles spread uniformly throughout both lungs, sometimes accentuated along the pleural surfaces, but not conglomerate or coalescent. The density of the millions of microliths is frequently sufficient to obscure the outlines of the heart and the diaphragm.

X-ray Visualization of the Intervertebral Disk. R. E. Wise, W. J. Gardner and R. B. Hosier. New England J. Med. **257**:6-10 (July 4) 1957 [Boston].

One hundred sixty-five patients are reported on, in whom 339 disks were injected. Of these patients 68 were operated on, with exploration of 107 disks. Disk protrusions were found in 55 patients at operation, and sciatic pain was produced by the injection in 38. Three basic diskographic patterns have been observed. The first, which is considered the normal pattern, is that in which a bilocular collection of dye is seen in both the anteroposterior and lateral views. The second pattern is the degenerative type, in which the contrast medium is spread throughout the confines of the disk in a flattened, disorganized manner. There is an associated narrowing of the interspace. The third pattern is that in which a protrusion is present in association with a tear or rupture of the annulus and the posterior spinal ligament; the pattern is usually of the degenerative type. There is no sharp line of demarcation between the simple degenerative disk and that with protrusion. It is apparently a matter of degree, with progression from degeneration without protrusion to progressively increasing protrusion until nerve-root pressure is produced and the classic clinical picture of a protruded disk is attained. Diskography has its advantages when compared with myelography. Iodopyracet is nontoxic and rapidly absorbed and obviates the necessity of removal, as is necessary with iophendylate. The occurrence of radiculitis and arachnoiditis, occasionally seen with myelography, is avoided. With diskography the disk itself is visualized, as opposed to myelography, which gives only indirect evidence. Myelography possesses the advantage of permitting a search for spinal cord or cauda equina tumors in addition to the search for disk protrusion. The diskogram is indicated in cases in which the myelogram is considered normal but symptoms remain suggestive of disk disease.

Calcification in Solitary Nodules of the Lung. M. E. O'Keefe, C. A. Good and J. R. McDonald. Am. J. Roentgenol. **77**:1023-1033 (June) 1957 [Springfield, Ill.].

The discovery of a solitary circumscribed nodular lesion in the lung, the so-called coin lesion, immediately raises the questions of its pathological nature. What diagnostic procedures should be carried out? How reliable are they? Should exploratory thoracotomy be done in all cases so that miscroscopic examination of the tissue can be made? A study of solitary nodular lesions removed surgically at the Mayo Clinic from 1940 to 1951 was made by Good, Hood, and McDonald. They concluded that a reliable sign of benignancy was the demonstration of calcification by roentgenologic study. The studies described here were undertaken to determine whether calcification may be present in a greater percentage of the solitary nodular lesions of the lung than has been detected on the usual preoperative stereoscopic and lateral roentgenograms and to learn whether special studies, as by laminography, would increase the incidence of detection of calcification in these lesions. In 149 of the 156 cases reported by Good, Hood, and McDonald, pathological specimens were available for further study. To this number the authors added 58 additional specimens from patients in whom pulmonary operations were performed at the Mayo Clinic for an isolated solitary nodule or circumscribed mass. Thus a total of 207 cases were available for this study together with the preoperative roentgenograms of the thorax.

Some 49.6% of the benign and 13.9% of the malignant lesions showed calcification by roentgenologic examination of the specimen. This study indicates that calcification is present and can be demonstrated by roentgenologic means in a greater number of cases than had been detected by the preoperative use of stereoscopic posteroanterior and lateral roentgenograms alone. The finding of calcium within these lesions does not, except for those showing the characteristic laminated and popcorn type of calcification, indicate that these lesions are benign. The fact that the granulomas which had a

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laminated appearance roentgenologically did not contain viable organisms seems to be a significant finding. The mere presence of calcium in roentgenograms of a lesion, unless of the laminated type, does not mean that the lesion is inactive bacteriologically. The number of laminagraphic examinations in cases in which pathological material was available was too small to evaluate this procedure as a diagnostic aid, but evidence indicates that it may often show calcification to be present that is not evident on the stereoscopic posteroanterior and lateral roentgenograms of the thorax. It is concluded from this study that a solitary circumscribed nodular lesion can be safely called "benign," from a roentgenologic standpoint, only if the laminated or popcorn type of calcification is clearly demonstrated.

Roentgenographic Recognition and Differentiation of Parosteal Osteogenic Sarcoma. G. M. Stevens, D. G. Pugh and D. C. Dahlin. Am. J. Roentgenol. **78**:1-12 (July) 1957 [Springfield, Ill.].

The authors report the occurrence of parosteal osteogenic sarcoma in 19 of 2,300 patients with primary tumors of bone seen at the Mayo Clinic up to May, 1956. Parosteal osteogenic sarcoma is an unusual type of primary, malignant, densely ossified tumor of bone that arises and proliferates from a juxtacortical position, thus providing a typical roentgenographic appearance, on which particular emphasis has been placed. The main distinguishing roentgenographic characteristics are the encircling, dense, lobular, and juxtacortical nature of growth, the failure of the lesion to destroy the cortex, the heterogeneity of ossification, and the failure to produce periosteal elevation. The presence of a thin free space between tumor and cortex is often seen with the proper degree of obliquity of the view. The tumors in 16 of the 19 patients involved the femur, and the distal part of the femur was the site in all but 2 of these.

The latest clinical follow-up on these 19 patients with parosteal osteogenic sarcoma revealed that 1 patient apparently was cured by local excision. Four patients had primary amputation and were alive and well, although 3 have had follow-ups of less than 5 years. Eight patients are living and well after one or more local excisions by amputation. Six patients were dead after local excisions and amputations. Recurrence of the tumor after local excision is almost universal, which is similar to the seeding problem observed in chondrosarcoma. The tumor usually re-forms in the image of the primary lesion.

The differential diagnosis of roentgenographically similar lesions includes consideration of such entities as myositis ossificans, osteochondroma, parosteal ivory osteoma, sclerosing osteogenic sarcoma, ossifying hematoma, and exuberant callus. Careful correlation of the history, roentgenographic features, and pathological characteristics is the best method of diagnosis. However, when pathological confirmation is lacking, the roentgenographic features in typical advanced cases are considered to be reliable enough to warrant serious consideration of amputation on roentgenographic appearance alone. If reasonable doubt as to the diagnosis exists and if the roentgenographic appearance is atypical, local excision might be attempted, to be followed by amputation if and when the first sign of recurrence is noted.

Ochronosis. M. M. Thompson Jr. Am. J. Roentgenol. **78**:46-53 (July) 1957 [Springfield, Ill.].

The author reports on a 63-year-old man with ochronosis due to alkaptonuria, a rare disease with severe, generalized arthritis, discoloration of cartilages within the body, and pigmentation of the eyes, the skin over the bony prominences, and the intima of the large vessels by deposition of ochre-colored granules. The urine voided by the patient was dark and turned black on standing in sunlight. The roentgenologic findings in the spine were those of osteoporosis and an accentuation of the normal kyphosis of the dorsal spine. There was ankylosis of the articular facets and the vertebral bodies of the lumbar and dorsal vertebrae. There was calcification of the intervertebral disks, most pronounced in the lumbar vertebrae. Advanced osteoarthritic changes were present in both hip joints with almost complete obliteration of the joint spaces and marked sclerosis of the femoral heads and the acetabulums. The superior portion of the head of the right femur was absent, and the remaining portion of the femoral head was markedly increased in density. The symphysis pubis was fused. The sacroiliac joints were almost fused, and there were extensive flocculent calcifications inferior and lateral to each ischial tuberosity. Examination of the knees showed very extensive osteoarthritic changes with marked narrowing of the joint spaces and advanced bony proliferation. The hands showed varying degrees of narrowing of the joint spaces of the phalanges and metacarpals, and there were many small cystic areas in the proximal phalanges adjacent to the proximal articular surfaces. There was extensive calcification of the cartilages of both ears. These roentgen findings confirmed those reported by Pomeranz and co-workers in 30 patients with ochronosis in the United States. Follow-up roentgenograms showed marked progression of the disease.

While almost all the cases of ochronosis are due to alkaptonuria, ochronosis also may occur after the external use of phenol and may be associated with the excretion of melanin in the urine. Alkaptonuria is a rare systemic disorder characterized

by the presence of alkaptone or homogentisic acid in the urine caused by an inborn error in metabolism of tyrosine and phenylalamine. These substances are only broken down as far as homogentisic acid, which accumulates in the blood and is excreted in the urine. Ochronosis appears at about an average age of 50 years, and the sexes are approximately equally affected. The disease lasts throughout the life of the patient. There is a definite hereditary tendency, and the incidence of alkaptonuria has been reported on the basis of Mendelian inheritance of recessive characteristics.

Fluoride Osteosclerosis. C. A. Stevenson and A. R. Watson. Am. J. Roentgenol. **78**:13-18 (July) 1957 [Springfield, Ill.].

The authors report on 23 patients between the ages of 44 and 83 years with fluoride osteosclerosis whose roentgenographic records were collected from 170,000 roentgenographic examinations of the spine and pelvis of patients living in Texas and Oklahoma, where many communities have excessive fluoride content in their drinking water. The 23 patients had been drinking water with a fluoride content for many years of from 4 to 8 ppm. In each patient, adequate clinical examination failed to establish any relationship between the roentgenologic findings and the clinical diagnosis of the patient's condition. Each of the patients had lived his entire life in the same fluoride-bearing area in which he was born. An attempt was made to grade the osseous changes on the basis of a 1 to 4 scale, with grade 1 showing bone density of a very minimal degree and grade 4 showing bone density of an extreme degree. Pelvic ligament calcification was graded also on the basis of the 1 to 4 scale, with grade 1 representing minimal calcification in either the sacrotuberous or sacrospinous ligaments and grade 4 showing calcification extending about 6 cm. from the ischium toward the sacrum. Fifteen of the 23 patients had this type of ligamentous calcification, and it closely paralleled the degree of bone density.

The authors' roentgenographic experience with bone changes noted in the 23 patients confirmed Roholm's observation in that the earliest changes of fluoride osteosclerosis occurred in the pelvis and the lumbar spine. These changes consisted of slightly increased bone density, always evenly distributed throughout the vertebral bodies, and appearing bilaterally and symmetrically in the pelvis. There was a definite but slight "ground glass" appearance. The most advanced changes consisted of a chalky-white appearance of the vertebral column and pelvis and in addition a slightly increased density and coarse trabecular pattern in the ribs. Calcification of the sacrospinous and sacrotuberous ligaments began at the ligamentous attachment in the pelvis, usually bilaterally and extended towards the sacrum for distances up to 6 cm. The entire length of the ligaments did not calcify, and no instance of calcification at the sacral end of the ligaments was observed.

Because of the nature of this type of sclerotic process with associated involvement of the pelvic ligaments and the absence of any abnormal blood changes, the differential diagnosis of fluoride osteosclerosis from other diseases producing increased bone density is not difficult. Fluoride osteosclerosis occurring in the patient exposed over a period of many years to fluorides as high as 8 ppm causes no harmful changes. Fluoride osteosclerosis is not evidenced roentgenographically in the patient drinking water with a fluoride content of less than 4 ppm.

Tuberculomas and Hamartomas of the Lung: Comparative Study of 66 Proved Cases. J. M. Bleyer and J. H. Marks. Am. J. Roentgenol. **77**:1013-1022 (June) 1957 [Springfield, Ill.].

Tuberculoma is a tumor-like granuloma caused by the tubercle bacillus, encapsulated by connective tissue, and showing no evidence of surrounding inflammation or spread. Hamartoma is a tumor-like formation in which there is an abnormal arrangement of the normal components of the organ from which it arises. Hamartomas may be found in almost any organ. In the lungs there are two types: (1) the adult type, which is a relatively small lesion, and (2) the infant or newborn type, which is a massive, diffuse process often occupying a lobe or even an entire lung. The roentgenologic aspects of 52 pulmonary tuberculomas occurring in 41 patients and 25 pulmonary hamartomas (20 parenchymal and 5 intrabronchial) are presented and correlated with the clinical, surgical, and histological findings. All tuberculomas were circumscribed and were located subpleurally. In 23 patients, the tuberculoma was clinically silent and was discovered on routine or survey chest films. In 14 patients, the history and the symptoms were referable to tuberculosis. In only 4 patients were the history, symptoms, and the physical signs suggestive of tuberculosis. The tuberculomas were removed by wedge resection in 26 patients, by segmental resection in 10, by lobectomy in 4, and by pneumonectomy in 1. The last patient had advanced tuberculosis. Lobectomies were performed either because of technical difficulties or because the gross appearance of the nodule suggested malignant neoplasm. Mycobacterium tuberculosis was found in 11 of the 41 patients with tuberculoma. The tuberculoma probably represents the most benign form of tuberculosis and in its early stages is rarely if ever accompanied by advanced tuberculosis. Such occurred only once among the 41 patients. This is perhaps due to the

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fact that with a few exceptions the patients in this series had their tuberculomas removed soon after they were discovered. The benignity of tuberculomas, however, is relative and lasts only until their capsule breaks down or until the cavity which precedes some of them reopens. They then discharge their contents into the bronchial tree, as occurred in 3 patients.

All 25 hamartomas in this series were solitary, sharply delineated, and without any roentgenographic signs of perifocal reaction. The 20 hamartomas of the parenchyma appeared on the posteroanterior roentgenograms peripherally in 15 cases and more centrally in 5 cases. The 5 intrabronchial hamartomas caused atelectasis of the respective pulmonary segment. The mass causing the obstruction was not visible on the plain roentgenograms. Three of the 5 patients with such obstruction were bronchoscoped prior to surgery. In 2 the hamartoma was seen. The intrabronchial hamartomas were accompanied by cough and expectoration in 4 patients and hemoptysis in 1. The parenchymal hamartomas were clinically silent and were detected during roentgenologic examinations. The parenchymal hamartomas were removed by wedge or segmental resection in 18 patients, while lobectomy was done in 2 because the frozen section seemed to indicate malignant neoplasm. The intrabronchial hamartomas necessitated lobectomy in 3 patients and pneumonectomy in 2. Hamartomas do not have distinct roentgenograms. Furthermore, they may be present when there is a malignant lesion in the lung or elsewhere in the body. This was the case in 4 of the patients observed by the authors.

PHYSIOLOGY

Monocalcium Disodium Ethylenediaminetetracetate ($Ca\text{-}EDTA\text{-}Na_2$) in Saturnism: Therapeutic Effect and Effect on the Urinary Lead Excretion: Experience with Rabbits Intoxicated Intravenously, Intramuscularly, and Subcutaneously. M. Salvini, U. Vidali and U. Scudier. Policlinico (sez. med.) **64**:82-99 (April) 1957 (In Italian) [Rome].

The authors studied the effect of monocalcium disodium ethylenediaminetetracetate ($Ca\text{-}EDTA\text{-}Na_2$) in 18 rabbits subdivided into 3 equal groups. The animals were 9 to 13 months old and weighed an average of 2,250 Gm. each. The animals of the first group were given intravenous injections of 3 mg. per kilogram of body weight of lead acetate for 5 days, then they were given intravenous injections of 10 mg. per kilogram of body weight of $Ca\text{-}EDTA\text{-}Na_2$ for the next 5 days. The animals of the second group were given intramuscular injections of 4 mg. per kilogram of body weight of lead acetate for 6 days; 3 of these animals were then given intravenous injections of $Ca\text{-}EDTA\text{-}Na_2$ for the next 6 days. Observations made in these last 3 animals showed that the extra amount of lead eliminated as a result of the treatment was very low; therefore, the dose of the drug was increased to 240 mg. per kilogram of body weight per day for 6 days. The animals of the third group were given subcutaneous injections of 24 mg. per kilogram of body weight of lead acetate for 6 days; 3 of these animals were then given injections of 240 mg. per kilogram of body weight of $Ca\text{-}EDTA\text{-}Na_2$ for the next 6 days. Marked excretion of lead in the urine was observed in all animals during the 6 days following the days in which the animals had been given injections of lead acetate. Intravenous injections of $Ca\text{-}EDTA\text{-}Na_2$ caused an increase in the amount of lead so excreted in the urine. Treatment with $Ca\text{-}EDTA\text{-}Na_2$, however, accounted only for a minimal part of the amount of lead that the animals excreted in the urine. The authors believe that $Ca\text{-}EDTA\text{-}Na_2$ causes decomposition of the lead in the tissues, a reduction of the toxic effect of the lead on certain tissues, and an increased transfer of chelate to the kidney.

In-Flight Hyperventilation During Jet Pilot Training. B. Balke, J. G. Wells and R. T. Clark Jr. J. Aviation Med. **28**:241-248 (June) 1957 [St. Paul].

The increasing number of unexplained jet aircraft accidents indicated a need for experimental investigation of possible physiological factors leading to a pilot's incapacity for safe flying. In addition to hypoxia, hyperventilation was suspected as being a possible cause for a critical deterioration of flying performance. Three hundred sixty-seven in-flight samples of mixed expired air were obtained from 29 pilots, whose average age was 22 years, during 125 flights in the course of their training phase in the T-33 type jet aircraft. Carbon dioxide tensions of these air samples were estimated by assuming a tidal volume of 850 cc. and a respiratory dead space of 250 cc., which represented the average values obtained in a laboratory study on 14 aviation cadets. The alveolar carbon dioxide tensions were then calculated according to the barometric pressure present at the moment of sampling. Similar determinations were made using 219 samples of mixed expired air which were obtained from 19 pilots, whose average age was 30 years, during 64 flights in the course of their training phase in the faster F-86 type jet aircraft, and 143 samples of air obtained from 17 pilots, whose average age was 33 years, during 41 missions in the course of their training phase in the still faster F-100 type jet aircraft. Results of in-flight sampling of expired air in the course of these 3 phases of jet training verified the existence of in-flight hyperventilation. Incidents of hyperventilation appeared to become more frequent with the increase in high-performance capabilities of the aircraft flown.

BOOK REVIEWS

Bronchopulmonary Diseases: Basic Aspects, Diagnosis and Treatment. By 142 authors. Edited by Emil A. Naclerio, M.D., Chief of Thoracic Surgical Services, Harlem and Columbus Hospitals, New York. Foreword by Richard W. Overholt, M.D., Director, Overholt Thoracic Clinic, Boston. Cloth. $24. Pp. 956, with 719 illustrations. Paul B. Hoeber, Inc. (medical book department of Harper & Brothers), 49 E. 33rd St., New York 16, 1957.

In the past decade, the field of bronchopulmonary disease has developed so rapidly that it is recognized as an integral part of internal medicine and thoracic surgery. Until recently knowledge of this subject was meager, and many patients died as a result of undiagnosed and untreated conditions in this field. Today, many of these patients may be cured and others improved and have longer life. The tremendous progress in fundamental knowledge has greatly facilitated the diagnosis and management of these diseases. The need for an up-to-date, compact, authoritative, and comprehensive compilation on diagnosis and treatment was the basic motive for preparing this volume. A unique feature is the emphasis on certain aspects of embryology, anatomy, physiology, and pathology essential to the understanding of this complex subject and the inclusion of principles of medical and surgical treatment. The practicing physician should be familiar with all facets of this developing field, calling for the combined efforts of physician, surgeon, radiologist, endoscopist, and anesthesiologist. In the first two sections, the book covers fundamentals in the management of asthma and emphysema; physiological and physiopathological mechanisms responsible for the sequence of events are described. The use of special drugs in bronchopulmonary diseases, the development of bronchospirometry, and pulmonary arterial catheterization in pulmonary function are reevaluated. In the section on diagnosis, clinical and laboratory procedures are discussed. Lung biopsy is emphasized and the reliability and pitfalls associated with x-ray diagnosis are pointed out. Certain important subjects are presented as individual monographs. Changes and modern evolution of our present concepts of tuberculosis, cancer, and many other diseases are amply dealt with. With few exceptions, no attempt was made to describe operative techniques, since these are found in books on surgery. The physician dealing with bronchopulmonary diseases must quickly gather evidence and make a wise decision. This volume should prove most helpful in this regard. The authors are all well qualified in their specialties.

The Care of the Expectant Mother. By Josephine Barnes, M. A., D.M., M.R.C.P., Assistant Obstetrician and Gynaecologist, Charing Cross Hospital, London. Cloth. $7.50. Pp. 270, with illustrations. Philosophical Library, Inc., 15 E. 40th St., New York 16, 1956.

The writer has tried to cover the subject of obstetrics briefly. This makes the book an abbreviated outline for guidance of persons with limited training in obstetrics. In general, the principles set down are acceptable, although there is disagreement with the statement that the first examination of a pregnant woman should be deferred until the 16th week because no important information can be obtained before this time and that it is difficult to reach the promontory of the sacrum until later in pregnancy. The procedure described for the Friedman test for pregnancy varies from that done in the United States, where only one injection of 10 cc. of filtered urine is given. In the United States, the blood pressure is not considered to be abnormally high when it is over 120/80 mm. Hg; 140/90 is the figure used in most clinics. The writer makes the common mistake of considering increased blood pressure as synonymous with toxemia. Too much space is devoted to the detailed description of the Rh factor. Likewise, in discussing edema in eclamptogenic toxemia, the author dilates on its presence in such unimportant locations as the lower extremities, hands, and face and fails to call attention to the critical importance of pulmonary and cerebral edema.

There is a good description of government-controlled obstetric service in Great Britain, including insurance benefits, maternity allowance, and priority in foods and supplements for expectant mothers. Abnormal pregnancy and labor are covered briefly. Occiput posterior and breech presentations are considered as malpresentations. The influence of the arcuate type of bicornuate uterus on transverse presentation is ignored, as is its connection with breech presentation, prematurity, and intrauterine fetal death. As in most modern textbooks, too much emphasis is placed on the value of x-ray pelvimetry for determining cephalopelvic disproportion as compared with careful estimation of the moldability of the fetal head and the effect of relaxing on increasing pelvic diameters during labor. It may be questioned that no 35-year-old primipara or a woman with a long period of infertility should be given a trial of labor but should have a cesarean section. The subject of anesthesia in obstetrics is hardly touched on; in the United States

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this would be considered a serious omission. The induction of labor in malpositions of the fetus and "especially in transverse lie or its recurrence after correction" would not be an acceptable teaching in most clinics in the United States. There is, under these circumstances, far too much danger of prolapsed cord.

The illustrations include retouched roentgenograms dealing with x-ray pelvimetry, twins, and a dead fetus; photographs showing abdominal palpation; and a distorted sagittal section drawing depicting the Hegar's sign of pregnancy. The drawings of the female bony pelvis are not well done and the embryologic drawings, with the exception of those showing the fetal circulation, leave much to be desired. In general, the format of the book is good. The type is clear and the outline form with italicized subheadings makes for ready reference.

Ciba Foundation Colloquia on Ageing. Volume 3: Methodology of the Study of Ageing. Editors for Ciba Foundation: G. E. W. Wolstenholme, O.B.E., M.A., M.B., and Cecilia M. O'Connor, B.Sc. Cloth. $6.50. Pp. 202, with 47 illustrations. Little, Brown & Company, 34 Beacon St., Boston 6; J. & A. Churchill, Ltd., 104 Gloucester Place, Portman Sq., London, W. 1, England, 1957.

This third volume maintains the same high standards of the two previous volumes. The earlier volumes dealt with general aspects and aging in transient tissues. In the current book, 12 subjects are reviewed by experienced investigators, and a summary of their personal researches is given. Each chapter includes an account of the discussion that followed the presentation of the paper. As those present, limited to 28, were persons with long experience in research in gerontology, the report may be accepted as the best current thought on the subjects presented. Much credit for the substance of this work is due Dr. Charles H. Best, of Toronto, who was the chairman, and to Dr. R. E. Tunbridge, of Leeds, England, who was a consultant.

The subjects, obviously selective, included: The Biological Approach in the Comparative Study of Ageing by Alex Comfort; The Study of the Ageing of Cells by J. F. Danielli; Studies on Adaptation as a Method of Gerontological Research by F. Verzar; Methods and Limitations in Studies of Human Organ System Function by M. Landowne; Nutrition, Liver Disease and Some Aspects of Ageing in Africans by T. Gillman; and Methodology of the Study of Intelligence and Emotion in Ageing by I. Lorge of Columbia University, New York City. The discussions by Verzar, Tunbridge, Gillman, and Lorge are especially noteworthy and stimulating to thought. The focus of attention on the biological factors involved at the cell level, including some references to genetics and the chemical processes involved, merits wide study. More people are living longer. The biology of aging is a fascinating field which will yield valuable information as the newer biological techniques are used and performance is scientifically evaluated. This volume on methodology is most timely, since many groups are establishing study centers for research in the field of aging. Reference to this small volume packed with data of first importance should prove exceedingly helpful. This work is highly recommended.

Practical Dermatology. By Samuel M. Peck, B.S., M.D., Dermatologist to Mount Sinai Hospital, New York, with Laurence L. Palitz, M.D., Ph.D. Cloth. $7. Pp. 380, with 122 illustrations. Landsberger Medical Books, Inc., distributed by Blakiston Division, McGraw-Hill Book Company, Inc., 330 W. 42nd St., New York 36, 1956.

This compact volume by two prominent dermatologists combines the features of a handbook and brief textbook of dermatology for practitioners. It deals with the more common dermatoses seen in practice and emphasizes diagnosis and treatment. The authors include such information on etiology and pathological physiology as they feel is necessary for a rational approach to therapy. This book presents the author's own views on the cause, mechanism, and treatment of the various dermatoses. In discussing therapy, they recommend only those measures with which they have had ample personal experience. These include the use of most of the many new agents available. The material is arranged in orthodox fashion and presented in a clear, concise, and readable manner. While many of the photographs are excellent, a number are lacking in clarity. The classification of hemorrhagic diseases should be expanded to include some of the more recently discovered disturbances of the clotting factors. This book, especially the sections on therapy, which include many prescriptions and detailed instructions for their use, should be useful to practitioners. The chapter on contact dermatitis and industrial dermatoses is particularly authoritative, since Dr. Peck has long been a leader in this field.

Medical Physiology. Edited by Philip Bard, Professor of Physiology, School of Medicine, Johns Hopkins University, Baltimore. [Formerly: Physiology in Modern Medicine, by J. J. R. Macleod.] Collaborators: Henry C. Bazett, and others. Tenth edition. Cloth. $14. Pp. 1421, with 438 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1957.

This new edition is the work of 13 authors. It contains extensive discussions of blood and circulation, respiration, the alimentary tract, metabolism and nutrition, the distribution and regulation of body fluids, endocrinology, the neuromuscular system, the central nervous system, and the special senses. There is no special section on reproduction. Some of the essential phenomena are dealt with in the chapters on the circulation and on endocrinology. The physiology of the skin is similarly represented by various passages in the sections on body fluids, circulation, and neurosensory mechanisms, and the physiology of the ureters and urinary bladder is mentioned in connection with the autonomic nervous system. The present edition of this work is probably most valuable for its thorough treatment of the physiology of the central nervous system and for its bibliography. It is well indexed.

QUERIES AND MINOR NOTES

RADIATION AND MASS X-RAY SCREENING

To the Editor:—*The United States Public Health Service has seemingly recommended against wide-scale use of chest x-rays for detecting tuberculosis except in certain areas where the incidence of tuberculosis is increased. The National Tuberculosis Association has submitted figures from both the National Academy of Sciences and the Brookhaven Laboratory, which give the amounts of radiation to the gonads from various x-ray procedures. It would seem that the amounts received through the use of routine chest x-rays during the reproductive period, while not negligible, are relatively insignificant. For many years there has been a compulsory program of yearly x-rays for all staff members and students at a university. Please elaborate on mass x-ray screening as a tuberculosis detection program.*

Paul C. Schumacher, M.D., Oxford, Ohio.

Answer.—It would not be correct to infer from recent articles in the press that the Public Health Service is "against mass x-ray screening." The Service is, however, urging public and private agencies to evaluate their present programs, so that they may utilize x-ray equipment more selectively and thus avoid subjecting large segments of the population to unnecessary radiation. Toward this end the Public Health Service recommends that emphasis be placed on x-ray screening of population groups that are known to be at the highest risk of contracting tuberculosis and, thus, can be expected to yield considerable numbers of new cases. Examples of such groups are contacts of open cases, persons admitted to hospitals, patients and employees in mental hospitals, inmates of correctional institutions, low economic groups (particularly those in slum areas), migrant laborers, alcoholics, and others.

This principle of selectivity, however, implies more than merely the choice of population groups to be surveyed. Selection of areas for screening activity should also be determined by the quality and quantity of follow-up services available in any given area, diagnostic and treatment facilities, costs, accessibility of personnel, and the community's potentiality for making a maximum utilization of survey findings. For population groups known to be at low risk, the Service recommends the tuberculin test as an initial screening device and the use of x-ray examinations among positive reactors only.

The Public Health Service, of course, has been keenly aware for years that there is a measure of radiation hazard involved in the use of x-ray machines. Indeed, the earliest publications of the tuberculosis program of the Public Health Service stressed the need to protect technicians, survey clerical personnel, and x-ray subjects from excessive radiation. Current findings that emphasize the significance of relatively low-level radiation exposure now serve to intensify former efforts of the Service to eliminate all unnecessary and avoidable radiation. Therefore, the Service urges the application of protective devices to x-ray equipment, such as screens, cones, and filters. Emphasis is also being placed on the need for systematic inspection of all x-ray case-finding equipment, particularly at a time immediately prior to the beginning of a survey and at frequent intervals thereafter. Early this autumn a national conference on this subject will be held in Washington. At its conclusion the Public Health Service expects to issue a more explicit policy.

THROAT IRRITATION FROM CLEANING TELEVISION TUBES

To the Editor:—*A patient, aged 38 years, who works in a television factory, has a chronic cough. X-ray has shown no evidence of active pathology, only healed lesions. The patient handles tubes which he washes with hydrofluoric acid (70%) and then with ammonium bifluoride; then he coats the tubes with a mixture of barium acetate, potassium silicate, and amyl acetate. Are these compounds dangerous to health, and can they be the cause of this patient's cough?*

Chester A. DeWitt, M.D., Silver Lake, Wis.

Answer.—Nothing in this query indicates the actuality of some exposure or the nature and degree of protection now existing. Assuming that some exposure takes place to either vaporous products or possibly dust in the making up of solutions, it may be urged that several of the constituents are well-known throat irritants and some are specifically toxic. Throat irritation may be associated with hydrofluoric acid, ammonium bifluoride, potassium silicate, and amyl acetate. Although amyl acetate may not be rated as highly toxic, it is outstanding as a

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

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throat irritant leading to coughing. Exposure levels below that of odor detection produce coughing in some persons. One reason why amyl acetate is regarded as nontoxic is that few persons will be willing to remain in any high-exposure area because of coughing. It is well known that hydrofluoric acid and ammonium bifluoride readily lead to skin damage if exposure exists. If well-designed protective exhaust systems are not now present, such may be in order.

DRUGS USED FOR TREATING TUBERCULOSIS

To the Editor:—*Has isoniazid or aminosalicylic acid any depressant effect upon spermatogenesis? Would pregnant mare's serum gonadotropin be contraindicated in arrested pulmonary tuberculosis?* *Hugh Clemmer, M.D., Lancaster, Calif.*

To the Editor:—*Will dihydrostreptomycin, aminosalicylic acid, or isoniazid, administered singly or in combination in the treatment of tuberculosis, cause hirsutism in women?*

Ralph L. Cash, M.D., Princeton, Ky.

These inquiries were referred to two consultants, whose respective replies follow.—Ed.

Answer.—There is not enough evidence to indicate whether any of the drugs used in the treatment of tuberculosis have a depressant effect upon spermatogenesis or cause hirsutism. Because aminosalicylic acid is a salicylate, it might have a slight cortisone-like action, but there is no clinical evidence of an effect as severe as hirsutism.

Answer.—No well-documented study has been found suggesting that isoniazid and aminosalicylic acid depress spermatogenesis or that pregnant mare's serum gonadotropin is contraindicated in arrested tuberculosis. No reference has been found to suggest that dihydrostreptomycin, aminosalicylic acid, or isoniazid, administered singly or in combination in the treatment of tuberculosis, cause hirsutism in girls or women.

PROPHYLAXIS OF RHEUMATIC FEVER

To the Editor:—*Please supply information on the current status of penicillin prophylaxis in rheumatic heart disease, specifically related to the duration of therapy after acute rheumatic fever. What is the treatment of adults who, on routine examination, are found to have rheumatic valvular heart disease without any previous history of acute rheumatic fever?*

Gerald Lieberman, M.D.,
West Los Angeles, Calif.

Answer.—Penicillin, given orally or by injection, in the form of benzathine penicillin G is considered the best form of prophylaxis in rheumatic heart disease. No one really knows how long prophylaxis should be continued after acute rheumatic fever. Since recurrences usually occur within five years after the initial attack, it was thought that five years of prophylaxis might be sufficient. However, since recurrences can occur after the five-year period, many investigators now believe that penicillin prophylaxis should be continued indefinitely.

As a general rule, adults who are found, on routine examination, to have rheumatic heart disease without any previous history of rheumatic fever are not put on penicillin prophylaxis. However, it is considered desirable to place those patients having frequent sore throats on penicillin prophylaxis. Also, if any of these individuals develop an acute upper respiratory infection which may be of streptococcic origin, prompt administration of penicillin by injection may prevent a possible recurrence of acute rheumatic fever.

FELDSPAR DUST

To the Editor:—*Is definite risk of silicosis associated with heavy or moderate exposure to feldspar dust, either in the grinding and processing or in the open mining? Also, is there the same or a similar increase in toxicity, related to the smaller particulate sizes of feldspar, as with some of the other silicates? Is masking indicated in certain processing operations, or is the necessity of masking dependent upon the particulate size?*

Daniel C. Wilkerson Jr., M.D., Bedford, Va.

Answer.—Feldspar is a silicate. It is a general name for a group of rock minerals corresponding to the general formulas, R′ $AlSi_3O_8$ and R″ $Al_2(SiO_4)_2$, where R=potassium, sodium, calcium, barium, etc. According to our present knowledge and from an epidemiologic viewpoint, it is an inert dust. The smaller the particle size, the greater the chance of its gaining entrance into the lung. The use of a mask or respirator is only one form of prevention. Whenever concentrations of any dust are heavy and exposure prolonged, a wetting-down process or removal of dust at its source by exhaust ventilation should be employed.

SUSTANCES TO INCREASE TANNING

To the Editor:—*Is bergamot oil harmful to the skin when used with some vehicle to promote tanning? Will lime juice aid the process of tanning?* *M.D., California.*

Answer.—Bergamot oil and lime juice contain chemicals which increase both the erythema and the pigment response of the skin to sunlight exposure. The active ingredient in these two natural products is a photodynamic furocoumarin, 5-methoxypsoralen. Since the concentrations of 5-methoxypsoralen in bergamot oil and lime juice may vary, the

response is unpredictable, the tanning produced is uneven and spotty, and, finally, marked erythema, edema, pain and vesiculation may occasionally occur. For these reasons essential oils and plant juices which contain photodynamic chemicals are not recommended for purposes of increasing tanning.

TESTICULAR ENLARGEMENT WITH LEUKEMIA

To the Editor:—*A 5-year-old boy with acute lymphocytic leukemia, type unspecified, has had a continuous clinical remission for two and one-half years. During this time he has had the continual administration daily of Cortone (25 mg.) and Purinethol (25 mg.). Recently the Cortone therapy was discontinued, and since then he has been found to have rapidly enlarging, firm testes that are slightly tender. There is a small pea-sized nodule in the epididymis of the left testis. The left testis is enlarging more rapidly and is already approximately twice the size of the right testis. There is no evidence of penile enlargement or other secondary sexual changes. On physical examination the patient is apparently well, with no evidence of a leukemia relapse. Except for generalized lymphadenopathy and mild Cushing's effect (from the steroids), he is otherwise in good health. The question of extensive investigation, including determination of rate of 17-ketosteroid excretion, biopsy of a testicular specimen, and bone marrow studies, in this boy presents a financial as well as a psychological problem. Might his basic disease or the previous therapy account for the enlarging testes? If not, what studies might be indicated at this time?*

H. H. Pride, M.D., Knoxville, Tenn.

This inquiry has been referred to two consultants, whose respective replies follow.—Ed.

Answer.—Nodular swellings are not uncommon in the course of leukemia. While the testis is an infrequent site of metastasis, the nodules probably represent localized infiltrations with leukemic cells similar to involvement of other organs, such as the liver, spleen, kidney, and nervous system. Often the appearance of nodular masses or the enlargement of the spleen represents an early manifestation of relapse in spite of a normal blood smear. Nothing would be accomplished by ketosteroid examinations except for academic interest. Of greater moment is the need for reexamining the bone marrow for evidence of relapse. The prolonged control of leukemia with minimal therapy in this case is worthy of note and reflects either the great variability in severity of this disease or an exceptional response to treatment. If the bone marrow should be found to be heavily involved with leukemia, therapy should be directed toward increasing the dosage of the steroids in the form of prednisone, 40 to 60 mg. daily, and/or a shift to Methotrexate, 2.5 mg. daily.

Answer.—Although not pertinent to the specific question regarding the probable cause for the enlargement of the testes, the fact that this child has exhibited a continuous clinical remission of symptoms and signs of acute lymphocytic leukemia for two and one-half years is worthy of comment. Such a remission must be considered as most unusual and may be an indication for review of the original hematological and bone marrow material upon which the diagnosis was based.

Colleagues with extensive experience in the use of hormone therapy and in conditions affecting the testes have not encountered a situation similar to that described in the inquiry. Although leukemia may affect any part of the body, a decision as to whether the enlargement of the testes in this instance is due to leukemia or to some separate or superimposed disorder cannot be answered with certainty without biopsy of a testicular specimen. If study of bone marrow reveals a picture compatible with leukemia, one might assume, with a fair chance of being correct, that the testicular involvement is due to leukemia. There appears to be no indication for a determination of the rate of 17-ketosteroid excretion in this case, but there does appear to be a definite indication for examination of bone marrow or biopsy of testicular tissue or both.

BROMSULPHALEIN IN SUBCUTANEOUS TISSUE

To the Editor:—*It is generally accepted that Bromsulphalein, as used intravenously for liver-function testing, is markedly toxic to tissues in concentrated solution, which may be observed if some of the dye gets out of the vein during intravenous administration. Would the chance of tissue necrosis be reduced by the immediate injection of hyaluronidase, local and/or systemic administration of hydrocortisone, application of icepacks, etc.? What is the recommended management of this situation?*

M.D., West Palm Beach, Fla.

Answer.—The best treatment of the irritating effects of Bromsulphalein on the subcutaneous tissues is their prevention. Bromsulphalein should be injected slowly and blood drawn into the injecting syringe intermittently to be sure that the needle is still in the vein. The injection should be discontinued as soon as there is indication that the dye is not being injected intravenously. If these precautions are observed, the small amount of dye that will occasionally be injected subcutaneously will produce no more than a stinging sensation and redness and local pain for 24 to 48 hours. In such a situation, elevation of the extremity and application of dry or moist heat is helpful. The necrosis produced from larger amounts of dye may be due to marked local vasospasm, and prompt subcutaneous injection of 1% aqueous procaine hydrochloride will dilute the dye, stop the pain, and reduce the likelihood of vasospasm. The procaine may be combined with hyaluronidase.

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ROUTINE USE OF VITAMIN K PREPARATIONS IN OBSTETRICS

To the Editor:—*For many years the routine use of vitamin K preparations such as Hykinone, administered intramuscularly to all patients admitted to the labor rooms of a hospital, has been a standing order for most obstetricians. Hykinone has been given regardless of the stage of labor, many patients receiving it only minutes before delivery. Is this more or less routine use of Hykinone one of the many things one starts using and continues using forever? Is it still considered to have some beneficial effect upon blood clotting in both mother and baby? Is it something that could be done without?* *Elwyn H. Welch, M.D., Pomona, Calif.*

Answer.—It has not been proved that there is any need for the routine use of any vitamin K preparation. Greenhill in "Obstetrics" (ed. 11, Philadelphia, W. B. Saunders Company, 1955, p. 849) says: "Sanford, Shmigelsky and Chapin maintain that vitamin K does not affect the frequency of hemorrhagic manifestations. In their series of 1693 patients, 711 of whom received vitamin K, there were just as many conjunctival, vaginal, petechial, cerebral and umbilical hemorrhages and instances of melena and cephalhematoma in one group as in the other. The mortality for the two groups was the same."

Potter emphasizes the following: 1. In the majority of infants the prothrombin time is prolonged during the greater part of the first week of life beyond that which is normal for the adult. 2. The administration of vitamin K to the mother prior to delivery or to the infant after birth will usually prevent the customary prolongation. 3. After prolongation has once occurred, administration of vitamin K will usually cause a return to normal. There is no proof, however, that a prolonged prothrombin time is a direct cause of hemorrhage. The early optimistic prophecies that vitamin K would prevent hemorrhage and reduce the mortality rates have not materialized. From a study of 13,190 cases observed at the Chicago Lying-in Hospital of the University of Chicago, Potter concluded that no decrease in infant or fetal mortality can be expected from the routine administration of vitamin K to all women during labor.

Since there is no specific treatment for cerebral hemorrhage and since vitamin K does raise the prothrombin value of the blood of the newborn infant within four hours of its administration, it should be given to all infants suspected of having cerebral hemorrhage. The average single dose of synthetic vitamin K given prophylactically to women is 2 mg. at least four hours before delivery. The same amount may be given to the baby after delivery, whether or not the mother received the vitamin. Sanford and associates recommend giving vitamin C to infants suspected of having cerebral hemorrhage, because they found this vitamin to be consistently low in newborn infants with cerebral hemorrhage. Greenhill recommends that in every prolonged labor or anticipated difficult vaginal delivery vitamin K should be given to the mother at least four hours before delivery.

SATURATED AND UNSATURATED FATTY ACIDS

To the Editor:—*Please explain in simple language just what are saturated and unsaturated fatty acids. How can one distinguish between them when consuming edible fats?* *M.D., Illinois.*

Answer.—When the carbon atoms in the chain of a fatty acid are all linked to adjacent carbon atoms by a single chemical bond, the fatty acid is said to be saturated. If, however, there exists between two carbon atoms two chemical bonds, the two carbon atoms are said to linked by a "double bond," and the fatty acid is said to be unsaturated. The more of such "double bonds" that exist in the chain of a fatty acid molecule, the higher is the degree of unsaturation. In general, but not always, fats that are liquid at room temperature are more unsaturated than those which are solid. The major biologically occurring saturated fatty acids are palmitic, stearic, and butyric acids. The major biologically occurring unsaturated fatty acids are oleic and linoleic acids. A notable exception to the rule of liquidity at room temperature is coconut oil, which contains primarily saturated fatty acids. The best way to know which edible fats are saturated and which unsaturated is to consult a table of composition, such as occurs in Bailey's "Industrial Oil and Fat Products" (New York, Interscience Publishers, Inc., 1951).

VACCINE PROPHYLAXIS FOR MICROCOCCIC AND STREPTOCOCCIC INFECTIONS

To the Editor:—*A patient with nephrosis is subject to micrococcic (staphylococcic) and streptococcic infections. Please evaluate the problems involved in developing a vaccine giving long-term immunity to the above bacteria.*

I. E. Cooper, M.D., Port Richmond, N. Y.

Answer.—It is generally agreed that vaccine prophylaxis or therapy of micrococcic infections is of questionable value. Active immunization with formalinized toxin (toxoid) has given promising results in the treatment of skin infections but not in infections such as chronic micrococcic osteomyelitis (MacDonald and Taylor: *Lancet* **2**:558, 1951). Pathogenic micrococci produce a number of hemolytic toxins, of which the α-toxin, which has leukocidin and dermonecrotic activity, and the δ-toxin, which has dermonecrotic activity, are associated with virulence. The α-toxin has been the most thoroughly investigated in connection with effective immunity. Preparation of the toxoid requires particular care to insure atoxicity and antigenicity

(Farrell: *J. Immunol.* **41**:119, 1941); commercial preparations are available. Dosage recommendations vary. Dolman (*J. A. M. A.* **100**:1007-1010 [April 1] 1933; *Canad. M. A. J.* **30**:601, 1934; *Canad. M. A. J.* **31**:130, 1934; *Lancet* **1**:306, 1935) recommends an initial dose of 0.05 ml., with weekly increases of 0.05 ml. until the eighth dose of 0.5 ml. is given. If a second course of inoculation is required, the patient should be rested for one or two months. The immunity is not of a high order, and antitoxin titers do not correlate well with clinical results. The immunity is not long lasting, and subsequent courses of inoculation may be required, as indicated by the condition of the patient. Coagulase (procoagulase) is associated with the virulence of micrococci, but is only feebly antigenic, and the efficacy of the immune response to it is not known. Nephrosis should not complicate the immune response.

Immunity to infection with β-hemolytic streptococci is associated with antibody to the type-specific M antigen present in the cell wall and not with antibody to streptococcic toxins (streptolysin O, streptokinase) other than scarlatinal toxin. Streptococcic vaccines are not at present of practical value because of the multiplicity of types and required polyvalency and because of the short (two to four months) duration of effective immunity. Recently M antigen has been prepared from sonic and other lysates of streptococci, but theoretically possible polyvalent mixtures of purified M antigen have not been prepared or tested. At the present time chemoprophylaxis, as with benzathine penicillin G, is the most effective prophylactic measure. The α-hemolytic streptococci (green-forming streptococci or streptococci of the viridans group) are antigenically heterogeneous, and prophylactic immunization with vaccines has not been extensively studied. Active immunization with any streptococcic vaccines requires consideration of the possible prior existence or development of hypersensitivity to streptococcic antigens.

TREATMENT OF NEUROSYPHILIS

To the Editor:—*Results of the Kolmer and Venereal Disease Research Laboratory tests on a 47-year-old patient are positive, and the colloidal gold curve for the cerebrospinal fluid is 555331000. The administration of penicillin was interrupted at 7,000,000 units because of severe exfoliative dermatitis and penicillin reactions. Please advise what less sensitive form of penicillin might be tried, or whether other antibiotics, such as tetracycline, Aureomycin, or chloramphenicol, might be used. What is the proper dosage of these drugs in dealing with syphilitic meningoencephalitis?*

Lawrence C. Cheng, M.D., Allentown, Pa.

Answer.—Information given in the query is not sufficient for a satisfactory judgment. However, one can conclude that penicillin should not be given again to this patient. Not knowing the nature of the "other penicillin reactions," one cannot judge whether a "less sensitive penicillin" should be tried. Such a trial is opposed unless the need becomes more urgent. Nothing is said as to the clinical status of this patient. If the patient had clinical evidence of neurosyphilis and this evidence has increased, indicating clinical progression of the disease, then one must consider the possibility of further treatment. However, from the absence of a positive statement one concludes that this is a case of asymptomatic neurosyphilis and that there is no clinical indication for further therapy at this time.

Without knowledge of the spinal fluid cell count any decision in this case is rather a guess. It is necessary to know what the count had been at the start of therapy and what it now is. If the cell count now is normal, there is no serologic indication for further treatment at this time. One would also like to know the dilution in which the Venereal Disease Research Laboratory reaction was found to be positive, but that point is not of critical significance. One can hardly make a diagnosis of "syphilitic meningoencephalitis" without more evidence than has been given in the query. The inquirer should be referred to Thomas's excellent textbook "Syphilis: Its Course and Management" (New York, Macmillan Company, 1949). If a decision based on further information leads to institution of further therapy, this consultant suggests a trial of Aureomycin given daily for about six weeks. The dose would be three or four tablets (250 mg. each) daily, depending upon the size, weight, and general health of the patient.

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UNILATERAL LYMPHEDEMA OF THE LEG

To the Editor:—*A boy, now 10½ years of age, has had a unilateral lymphedema of the left leg below Poupart's ligament for almost seven years. This had its onset insidiously at the age of 3 years. About 10 days after the onset the patient had a slight leukocytosis, with 11,100 leukocytes per cubic millimeter, and eosinophilia of 17%. There was a low-grade fever for a few weeks; the tuberculin test was negative. Is there anything new about the etiology or the treatment of this troublesome, rare condition?*

Charles L. Concklin, M.D., Corpus Christi, Texas.

This inquiry has been referred to two consultants, whose respective replies follow.—Ed.

Answer.—This child has congenital lymphedema of the left leg. The etiology of this condition is unknown, and there is no satisfactory treatment. Fortunately, it is usually benign, and no serious complications are likely. To prevent attacks of lymphangitis, it is desirable to keep the web spaces between the toes sterile by daily application of Zephiran or some other antiseptic agent. Elevation of the leg at night and, when possible, during the day helps a little to prevent swelling. An elastic support is of no value, but a nonelastic stocking may be of some help.

ANSWER.—The condition described seems to be one of the variations of familial or hereditary edema which go under the heading of Milroy's disease. No one knows the cause, although it has been speculated that the disease can be acquired after an inflammatory reaction in the major lymphatics of the limbs. This is particularly suggested when it is unilateral. This consultant knows of no advances in treatment for this most puzzling situation. Its gross deformation can be somewhat alleviated by the application of a tight elastic stocking put on after the leg has been elevated for some hours. Of course, this is a makeshift, usually unsatisfactory procedure, although it may do some good. No attempts at corrective surgery have been successful.

INSOMNIA

TO THE EDITOR:—*A patient, past 45 years of age, complains of insomnia. He states that he has no difficulty falling asleep but wakes after one to three hours from a deep sleep; it then takes him one to two hours to fall asleep again. His physical condition is entirely normal, and he has no obvious tension of any kind. Please make suggestions as to treatment.* *Sidney Schreiber, M.D., Berwyn, Ill.*

ANSWER.—This is a very common condition and yet still very difficult to treat. It is hard to conceive that there is not something tending to unsettle this man's sleep. In the absence of physical disease, an emotional stress may well be operating. Frequently the patient is not conscious of this stress, but occasionally it will be apparent to an outside observer who reviews his life. Recognition of this stress may solve the problem.

In management, reassurance frequently suffices, and the knowledge that the body regulates the amount of sleep necessary. It is more commonly the causative nervous tension which leads to fatigue rather than the actual lack of sleep. References to the sleeping habits of men like Edison may be helpful. Occasionally some of the longer-acting barbiturates or chloral hydrate may give the desired effect, without habituation or hang-over. Certainly they are worth a trial.

PURE WHITE FINGERNAILS

TO THE EDITOR:—*A 5-year-old child, except for defective hearing, has developed normally. However, for the past two years it has been noticed that her fingernails are all pure white in color without being brittle. No other members of the family have this condition. Please explain the significance of this phenomenon.* *M.D., New York.*

ANSWER.—Leukonychia totalis is a very rare condition, and, when it occurs at the age of 5 years, it must be seriously considered as being congenital in origin. It is not symptomatic of any particular organic disease. Occasionally trauma is associated with leukonychia punctata. Sabouraud once thought that this syndrome when found in so-called weak people was an early sign of tuberculosis, but there has been no clinical justification for that belief from the work of a good many observers. Lerner has postulated that it may sometimes be associated with a symptomatic metabolic disorder, which responded to high doses of ammonium chloride and to other substances which affect a shift in the acid basic balance in the direction of acidosis. Eller and Anderson have reported a case of nonapparent etiology in a girl 15 years of age. Sometimes the syndrome appears only temporarily. Pardo-Costello has observed a case in a patient having leprosy. However, it can be said that leukonychia totalis has not as yet been associated with any definite organic disease. It might be interesting, by way of ruling out a rare case of fungous infection, to secure a small portion of nail for microscopic examination; the finding of fungi, however, would be rare indeed. Thus, it must be concluded that leukonychia totalis is apparently of hereditary or congenital etiology, and to date there is nothing in the way of treatment that can be offered.

INHALATION OF BARIUM CARBONATE

TO THE EDITOR:—*In the manufacture of tile blocks, a local refractory recently used, for the first time, barium carbonate at a certain stage in the manufacture. The men working with this material noticed an unusual amount of dust and experienced burning in the throat, which persisted for several weeks. However, there have been no gastrointestinal or other symptoms; no chest x-rays have been done. This is the first time that barium carbonate has been used in this refractory, and the owners are interested in using it again. Is there any known toxic effect from inhaling barium carbonate dust?*

David L. Miller, M.D., New Bethlehem, Pa.

ANSWER.—Barium carbonate, as far as is presently known, causes no systemic injury by inhalation. Exposure to this dust can cause irritation to the nose and throat. This could be avoided by the utilization of proper protection.

COFFEE TO RELIEVE ACHING AND FATIGUE

TO THE EDITOR:—*How does a cup of coffee relieve the morning aching associated with chronic fatigue?*

M.D., Georgia.

ANSWER.—Coffee does not have any analgesic properties. The aching associated with chronic fatigue is probably on the basis of sustained muscle tightness and is probably associated with some reduction in blood flow through the muscles. Coffee probably acts in two ways: (1) As a central nervous system stimulant, it prods the patient to activity, and therefore there is in-

creased blood flow through the muscles and reduction of the muscle tightness associated with inactivity; (2) as a warm fluid with a deep tradition of psychological significance, it probably exerts a powerful placebo action.

PROPHYLACTIC TREATMENT OF PATIENT EXPOSED TO VENEREAL DISEASE

To the Editor:—*What is the proper medical management of a symptomless patient exposed to known venereal disease? Has chemoprophylaxis been definitely demonstrated to be effective in such a condition? Please give recommended prophylactic dosage for syphilis and gonorrhea.*

Harry E. Zion, M.D., Pullman, Wash.

Answer.—Due to the availability, safety, and low cost of penicillin, prophylactic treatment of venereal disease is indicated before clinical manifestations appear or a diagnosis is made. However, employment of this procedure makes a careful follow-up period of at least one year mandatory. Physical examinations and serologic tests are required. If the treatment does not eradicate the disease, it may merely mask it, leading to the development of late complications or infectious relapse. The recommended dosage varies with each authority. However, a single intramuscular injection of 2,400,000 units of procaine penicillin is considered to be adequate by most.

SURGICAL TREATMENT OF CHRONIC ANGINA PECTORIS

To the Editor:—*Do surgeons in this country perform ligation of the internal mammary arteries in severe cases of chronic angina pectoris not amenable to medical treatment? Italian surgeons are said to perform this operation with marked success and in many cases with almost complete abolishment of atrocious anginal pains.*

Joseph A. Belott, M.D., Port Orange, Fla.

Answer.—Technically, surgical treatment of chronic angina pectoris is easily done, and there should be some local surgeon who can perform the operation. The popularity of this operation is based upon the fact that it is such a simple procedure. However, physiological tests have not as yet been made as to whether the operation improves the coronary circulation. Physicians familiar with the coronary circulation cannot understand the rationale of it. The benefit that the patients say they have might be based on psychological reasons. If the circulation in the heart is actually improved by this operation, it should be possible to demonstrate improvement by various tests in the experimental laboratory. So far these tests do not exist.

DIABETES WITH HEMOPHILIA

To the Editor:—*Are there any cases on record of diabetes in patients with hemophilia?*

S. B. Ross, M.D., Brewster, N. Y.

Answer.—Careful search has disclosed no recorded case of diabetes in an individual with hemophilia. However, such a combination might by chance occur rarely, and a more exhaustive review of the literature might reveal such.

TOXICITY OF GRAPHITE

To the Editor:—*In the query and minor note on toxicity of graphite in the issue of* The Journal *for Aug. 10, 1957, page 1727, it is stated that there is no evidence that graphite affects the respiratory tract. Graphite pneumoconiosis is a recognized condition, characterized by nodular masses sometimes containing cavities filled with a suspension of graphite in fluid. The clinical manifestations are described as similar to "slowly developing silicosis," with a radiologic picture resembling pneumoconiosis of coal miners. Graphite pneumoconiosis is compensable in Great Britain (Hunter: Diseases of Occupations, London, English Universities Press, 1955, pp. 187, 854).*

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The above comment was referred to the consultant who answered the original query, and his reply follows.—Ed.

To the Editor:—*It is quite true that any dust might cause changes within the lung to be noted by x-ray, provided that there is a prolonged exposure to severe concentrations of dust of minute particle size. It is also true that instances of graphite pneumoconiosis have been reported in the literature, almost entirely from the British medical journals. There is reason to believe that there must have been present in these cases a percentage of free silica or that they represented (as observed by McCord) "only accumulation of graphite itself without tissue response."*

Graphite is used extensively in American industry, and, if it were per se a cause of pneumoconiosis, the incidence should be high enough to attain cognizance. If one were to agree that it can cause a pneumoconiosis, then one must also state that within present experience it would be a benign pneumoconiosis. For an excellent review of the subject, the reader is referred to McCord's article "Graphite (Plumbago, Black Lead), as a Source of Dusty Lung Disease" (Indust. Med. 18:483, 1949).

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